

This gene is expressed primarily in keratinocytes and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integumentary, or neurological and behavioural disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. brain, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or detection of neurodegenerative disease states and behavioural disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Alternatively, expression within keratinocytes indicates polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athlete's foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chondromalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia

congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

- 5 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:73 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.
- 10 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 535 of SEQ ID NO:73, b is an integer of 15 to 549, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 64

- 20 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
LCSTPVPTLFCPRIVLEVLVVLRSISEQCRRVSSQVTVASELRHRQWVERTLSR
QRQNYLR (SEQ ID NO:366). Polynucleotides encoding these polypeptides are also encompassed by the invention.

- 25 This gene is expressed primarily in osteoclastoma.
- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal disorders, and diseases of the haemopoietic and immune system, particularly cancer. Similarly, polypeptides and antibodies directed to these
- 30 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the bones, immune and haemopoietic system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.skeletal.hematopoietic, and cancerous and wounded tissues) or bodily fluids
- 35 (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard

gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:223 as residues: Ser-59 to Glu-67.

5 The tissue distribution in osteoclastoma tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the bones, immune and haemopoietic systems and cancer. Moreover, the protein may play a role as a therapeutic in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well
10 as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chondromalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders. For example, in rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia
15 congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available
20 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:74 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more
25 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 576 of SEQ ID NO:74, b is an integer of 15 to 590, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 65

When tested against dermal fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) promoter
35 element. Thus, it is likely that this gene activates fibroblast cells through the EGR1 signal transduction pathway. EGR1 is a separate signal transduction pathway from Jak-STAT. genes containing the EGR1 promoter are induced in various tissues and cell

types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

5 ARGETAYDGAAVEFQEPLSSCLFSSLNPHHWPTLGVGRPVMILTLEDKD (SEQ
ID NO:367), ELLQCQMLEASTLIHLHHPRPGFPALCSFLGFRHHLHHDALCIRV
LPEDLEAKLCVSLHQLLHRGLCLPGFGAACPGDQGSEDEARPPAVLRAVALLR
AGLRHLSVHSGWYHLPH SRNGLPLLALVVHFPEYGGGPREPVPQGSG
EFGRTELSTKGDTGDSRNSHLAQDMASLPFFKPCECTHV AVCSPPHPLCQ
YLCL (SEQ ID NO:368), LQCQMLEASTLIHLHHPRPGFPALCSFL (SEQ ID
10 NO:369), HQLLHRGLCLPGFGAACPGDQGSEDEARPPA (SEQ ID NO:370),
and/or LALVVHFPEYGGGPREPVPQGSGEFGR (SEQ ID NO:371) .

Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in testes.

Therefore, polynucleotides and polypeptides of the invention are useful as
15 reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, male reproductive and endocrine disorders, cancer, particularly testicular
cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful
in providing immunological probes for differential identification of the tissue(s) or cell
20 type(s). For a number of disorders of the above tissues or cells, particularly of the male
reproductive and endocrine systems, expression of this gene at significantly higher or
lower levels may be detected in certain tissues or cell types (e.g. reproductive, testes,
endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, seminal
fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell
25 sample taken from an individual having such a disorder, relative to the standard gene
expression level, i.e., the expression level in healthy tissue or bodily fluid from an
individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID
NO:224 as residues: Lys-53 to Leu-60, Pro-94 to Gln-99, Ser-176 to Gly-184, Ser-
30 199 to Val-207.

The tissue distribution in testes, combined with the detected EGR1 biological
activity indicates that polynucleotides and polypeptides corresponding to this gene are
useful for the diagnosis and treatment of male reproductive and endocrine disorders,
including aberrant testicular function (e.g. endocrine function, sperm maturation).
35 Moreover, in light of the EGR1 activity, it may also be useful in the diagnosis and
treatment of a variety of proliferative disorders, especially testicular cancer. Protein, as

well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:75 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1042 of SEQ ID NO:75, b is an integer of 15 to 1056, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or equal to a + 14.

15 FEATURES OF PROTEIN ENCODED BY GENE NO: 66

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: QSWTAPAARLPMALPQMCDGSHLASTLRYC (SEQ ID NO:372), QSAAQFWWPGRSASLGGAKGMQPPSLASWPXPRSIRCL RAPAPC SXPSASSAAVQVACCCSLACCGPSRPASQGHLRWDPYHLSRDLYYLTVESSEK ESCRTPKVVDI PTYEEAVSFPVAEGPPTPPAYPTEEALPSGSRDALLSTQPA WPPPSYESISLALDAVSAETTPSATRSC SGLVQTARGGS (SEQ ID NO:373), GSTGLWRGDRGPIEGGPGMLAL TDHSRVSFPVAEGPPTPPAYPTEEAL EPSGSRDALLSSVXGASWPGWAVASPSLHQAKQSVPATRTTVPLTVM Q (SEQ ID NO:374), QWFWWPGRSASLGGAKGMQPPSLASWP (SEQ ID NO:375), SSAA VQVACCCSLACCGPSRPASQGHLRW (SEQ ID NO:376), VSFPVAEGPPTPPAYP TEEALEPSGSRDALLS (SEQ ID NO:377), and/or RVSFPVAEGPPTPPAYPTEE ALEPSG (SEQ ID NO:378). Polynucleotides encoding these polypeptides are also encompassed by the invention.

30 This gene is expressed primarily in pituitary gland.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine disorders, such as dwarfism. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this

gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. endocrine, immune, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard
5 gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in pituitary indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of disorders of the pituitary gland and endocrine system. Moreover, considering the vital
10 importance of the pituitary in serving as a master regulator for various endocrine glands, the protein product of this gene would also be useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g. diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-,
15 hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-, hypoparathyroidism), hypothalamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available
20 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:76 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more
25 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 916 of SEQ ID NO:76, b is an integer of 15 to 930, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 67

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

35 SNEILLSFPQNYIQLNGSLIHGLWNLASLFSNLCLFVLMPPFAFFFLSEGFAGLKKGIRARILETLVMLLLLALLILGIVWVASALIDNDAAS (SEQ ID NO:379).

Polynucleotides encoding these polypeptides are also encompassed by the

invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

5 This gene is expressed primarily in the developing brain, liver and heart, and to a lesser extent, in cancerous tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, neural, hepatic, or cardiopulmonary and haemopoietic disorders, in addition to cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the fetal tissues and the haemopoietic and neural systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developmental, neural, hematopoietic, hepatic, cardiovascular, pulmonary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, bile, serum, pulmonary surfactant or sputum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:226 as residues: Glu-67 to Asn-74, Glu-88 to Asn-93, Lys-95 to Ser-105, Arg-152 to Ala-164, Ala-204 to Arg-210, Phe-254 to Thr-262, Pro-295 to His-311.

The tissue distribution in developing brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of haemopoietic and developmental diseases and cancers. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or

neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Alternatively, the relatively specific expression of this gene product during
5 embryogenesis indicates that it may be a key player in the proliferation, maintenance, and/or differentiation of various cell types during development. It may also act as a morphogen to control cell and tissue type specification. Because of potential roles in proliferation and differentiation, this gene product may have applications in the adult for tissue regeneration and the treatment of cancers, which include, but are not limited to
10 the following tissues or cells: pulmonary, immune, neural, hematopoietic, or hepatic tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ
15 ID NO:77 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of
20 a-b, where a is any integer between 1 to 4449 of SEQ ID NO:77, b is an integer of 15 to 4463, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where b is greater than or equal to a + 14.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 68

The translation product of this gene shares sequence homology with a putative yeast transmembrane protein which may play an important role in intercellular signalling, intracellular transport, or regulation of cellular homeostasis. In specific
30 embodiments, polypeptides of the invention comprise the following amino acid sequence: PTRPVLLLAINGVTECFTEAAMSKEEVDRYNFV (SEQ ID NO:380), and/or NDKKLLFLKGFWSSLKNETPPPHFRLRMVTGVSCSGTLWCLISGV AVTPLQSPQWG SYTECVPTTELPIAGPGASGVQASLKSRHFVSASGHT (SEQ ID NO:381). Polynucleotides encoding these polypeptides are also encompassed by the
35 invention.

This gene is expressed primarily in pulmonary, immune cells, epididymus, and testis tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the reproductive organs, immune, and pulmonary systems, in addition to endothelial and epithelial tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, respiratory and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. pulmonary, immune, reproductive, testes, epididymus, endothelial, epithelial, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, seminal fluid, pulmonary surfactant or sputum, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:227 as residues: Arg-45 to Thr-52, Tyr-60 to Gly-66, Ala-87 to Trp-92, Leu-105 to Ser-115.

The tissue distribution and homology to putative transmembrane protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases of the reproductive, pulmonary and immune system. Moreover, the protein product of this gene may be useful in the diagnosis, treatment, and/or prevention of a variety of male reproductive disorders, which include, but are not limited to, aberrant testicular function, male sterility, impotence, or related endocrine disorders. Protein may also serve a role as a contraceptive. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:78 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 777 of SEQ ID NO:78, b is an integer of 15 to

791, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where b is greater than or equal to a + 14.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 69

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

SENRIYRNGLEKMRREVTIGRSSICLDQQVKAGNAVHHQWLKYVCWMVVVV

10 GSGVGDGG NLGM (SEQ ID NO:382). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in PMA induced T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
15 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as inflammatory or immunodeficiency conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,
20 particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene
25 expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:228 as residues: Ser-62 to Thr-73, Phe-80 to Gln-88.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides
30 corresponding to this gene are useful for study and diagnosis of immune system disorders. More specifically, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved
35 in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease.

sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus
5 erythematosus, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or
10 immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:79 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the
15 scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1278 of SEQ ID NO:79, b is an integer of 15 to 1292, where both a and b correspond to the positions of nucleotide residues shown
20 in SEQ ID NO:79, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 70

25 This gene is expressed primarily in monocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, which include, but are not limited to, leukemias, lymphomas, AIDS, arthritis and asthma. Similarly, polypeptides and
30 antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types
35 (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard

gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in monocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, immunodeficiencies (e.g. AIDS), immuno-suppressive conditions (transplantation) and hematopoietic disorders. In addition this gene product may be applicable in conditions of general microbial infection, inflammation or cancer. Moreover, this gene may also be useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:80 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1269 of SEQ ID NO:80, b is an integer of 15 to 1283, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 71

When tested against dermal fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) promoter element. Thus, it is likely that this gene activates fibroblast cells through the EGR1 signal transduction pathway. EGR1 is a separate signal transduction pathway from Jak-

STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

- 5 NWSGRRLRMWPSAALSPAVSSPALALTSPPKPLKGEVWLRWKLLGSRAVGLF
AF IALGTQSPLLHRACLPVRQSWGCESEHKAYPILRLQPDLETQVGPGHGVN
WDLRTQIRTIGELGGDGGCSE MRPLF (SEQ ID NO:383), and/or NLFSTPCKRQ
KLIKLEWTEAPNVALRCSLSCSLIPGLSPDLSSEAPEGRSVAKMEIARQQSCWL
VCI YCFRNPESTLAPGLPACEAELGLLRAQGLPHPASPARLGNTGGAWPR
10 SKLGSQNTN (SEQ ID NO:384), SSPALALTSPPKPLKGEVWLRWKLLG (SEQ
ID NO:385), EHKAYPILRLQPDLETQVGPGHGVNWDL (SEQ ID NO:386), and/or
ALRCSLSCSLIPGLSPDLSSEAPEGRSV (SEQ ID NO:387). Polynucleotides
encoding these polypeptides are also encompassed by the invention. The gene encoding
the disclosed cDNA is believed to reside on chromosome 11. Accordingly,
15 polynucleotides related to this invention are useful as a marker in linkage analysis for
chromosome 11.

This gene is expressed primarily in placenta.

- Therefore, polynucleotides and polypeptides of the invention are useful as
reagents for differential identification of the tissue(s) or cell type(s) present in a
20 biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, developmental anomalies, fetal deficiencies, pre-natal disorders and
cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful
in providing immunological probes for differential identification of the tissue(s) or cell
type(s). For a number of disorders of the above tissues or cells, particularly of the
25 reproductive system, expression of this gene at significantly higher or lower levels may
be detected in certain tissues or cell types (e.g. reproductive, placental, and cancerous
and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma,
urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an
individual having such a disorder, relative to the standard gene expression level, i.e.,
30 the expression level in healthy tissue or bodily fluid from an individual not having the
disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID
NO:230 as residues: Gly-22 to Gly-29, Gln-37 to Ala-44.

- The tissue distribution in placental tissue, combined with the detected EGR1
35 biological activity indicates that polynucleotides and polypeptides corresponding to this
gene are useful for the treatment and diagnosis of developmental anomalies, fetal
deficiencies and pre-natal disorders. In addition it may be useful in the detection and

treatment of ovarian and endometrial cancers. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:81 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 694 of SEQ ID NO:81, b is an integer of 15 to 708, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 72

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

LAPECCCGSVTYPRALVPRPCCPEPRAPLQLTLGLFSANPVNASPWGRCRSRR
GRGNLPLGHPVSTAFSSGDS (SEQ ID NO:388), and/or NTLHSKLVPSVYHSTE
KSCLV CFGMCPSIYKKMKSVLLIGTRMLLWLSHISQGPRPEAVLPRAPSP
SAAHPWL VFRKPGKRKPLGQM QKQK REGKPASGSPC (SEQ ID NO:389), YPR
ALVPRPCCPEPRAPLQLTLGLF (SEQ ID NO:390), and/or VLLIGTRMLL
WLSHISQGPRPEAVLPR (SEQ ID NO:391). Polynucleotides encoding these
polypeptides are also encompassed by the invention. The gene encoding the disclosed
cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to
this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in infant brain, and to a lesser extent, in placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developmental and neurological

systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, developmental, neural, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:231 as residues: Thr-45 to Arg-50.

The tissue distribution in fetal brain and placenta indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis and treatment of various developmental and neurological disorders and diseases. The protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:82 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1450 of SEQ ID NO:82, b is an integer of 15 to 1464, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:82, and where b is greater than or equal to a + 14.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 73

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

WIIVMFGKVLKIKDFMSTYSHTYTHTHMHAHTHTHTLTLSSLQNVLTLVAISDS
 15 DK ALLIF (SEQ ID NO:392), MTLLIAEKTWRRPWPCQWGYLGAEGDRHLEG
 RSLSLRHLQGAETPVLNPDLQLPSHIGKQAWSH ALGSL (SEQ ID NO:393),
 MSTYSHTYTHTHMHAHTHTHTLTLSSL (SEQ ID NO:394), and/or GAEGDRHLE
 GRSLSLRHLQGAET (SEQ ID NO:395). Polynucleotides encoding these polypeptides are also encompassed by the invention.

20 This gene is expressed primarily in the spleen of patients with lymphocytic leukemia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, lymphocytic leukemia and other cancers, as well as immune disorders such as AIDS, arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in spleen tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of

lymphocytic leukemia and other cancers, as well as other immune disorders and conditions including, AIDS, arthritis, asthma and microbial infection. Furthermore, the protein product of this gene may be useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:83 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 602 of SEQ ID NO:83, b is an integer of 15 to 616, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 74

When tested against Jurket and fibroblast cell lines, supernatants removed from cells containing this gene activated both the GAS (gamma activating sequence), and the EGR1 (early growth response gene 1) promoter elements. Thus, it is likely that this gene activates immune or fibroblast cells through the JAK-STAT and/or EGR1 signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation

of cells. EGR1 is a separate signal transduction pathway from Jak-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid

5 sequence: VVEPGLKASLGA

MSTLFPSLFPRVTETLWFNLDRPCVEETELQQQEQQHQA WLQ SIAEKDNNLVPI
GKPASEHYDDEEEEDD EDD EDE DSEEDSEDD EDDMQDMDEMNDYNESPDDGEVN
EVDMEGNEQDQDQWMI (SEQ ID NO:396), LFPRVTETLWFNLDRPCVEETEL
(SEQ ID NO:397), and/or YNESPDDGEVNEVDMEGNEQDQD (SEQ ID NO:398).

10 Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in cells of the immune and haemopoietic
15 systems, and to a lesser extent, in several other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and haemopoietic disorders, such as multiple myeloma,
20 immunodeficiencies, and inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and haemopoietic systems, expression of this gene at significantly higher or lower levels may be detected in certain
25 tissues or cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

30 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:233 as residues: Pro-21 to Gly-30.

The tissue distribution in immune tissues and cells, combined with the detected GAS and EGR1 biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the
35 immune, haemopoietic, and integumentary systems. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia.

thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis. therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:84 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 914 of SEQ ID NO:84, b is an integer of 15 to 928, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 75

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: MGFDIHGV LGEAVAEPREKKQE RAKWAPHDYDDPSLS LQDLLISWMISTWLIPMWKCQATIWFS LIQRLLNAYCMPGNFRHWEIAANTTN KT PGLMDFKFL (SEQ ID NO:399), EPREKKQERAKWAPHDYDDPSLSLQDL (SEQ ID NO:400), and/or MPGNFRHWEIAANTTNKT PGLMDF (SEQ ID NO:401). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on the X chromosome. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for the X chromosome.

This gene is expressed primarily in fetal liver and spleen, and to a lesser extent, in prostate cancer and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, reproductive, immune, and haemopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and developing systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developmental, hepatic, reproductive, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, bile, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in developing and immune tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of disorders of the haemopoietic and developing immune systems. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Moreover, the expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. The protein may also show utility in the treatment or diagnosis of various hepatic or reproductive disorders, which include, but are not limited to hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells, and prostate cancer, and/or congenital defects such as X-linked conditions. Protein, as well as, antibodies directed against the

protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:85 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 709 of SEQ ID NO:85, b is an integer of 15 to 723, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85, and where b is greater than or equal to a + 14.

15 FEATURES OF PROTEIN ENCODED BY GENE NO: 76

This gene is expressed primarily in fetal spleen and Wilm's tumor.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, haemopoietic, immune, developmental, or renal disorders, such as congenital defects, multiple myeloma, or Wilm's tumor. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the haemopoietic and developing systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developmental, immune, hematopoietic, renal, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the haemopoietic and developing systems and cancer. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the

production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:86 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 556 of SEQ ID NO:86, b is an integer of 15 to 570, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 77

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS

element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in induced T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as
5 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and inflammatory diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders
10 of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard
15 gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of immune and inflammatory diseases. The
20 secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines;
25 immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility);
30 chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding
35 nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:87 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 625 of SEQ ID NO:87, b is an integer of 15 to 639, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 78

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: QSVSPPLAPPLPPSLPSFLTETRSHYVARLVNSWAQM ILLPWPLKVLGLDVSHCAWPKSVFLQAMEEIAFCLFSVKYQVSSMTCF DRT SYMKNTYL (SEQ ID NO:402), and/or LFTETRSHYVARLVNSWAQMILLPWP (SEQ ID NO:403). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in bone marrow.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, anemias (leukemias), immune deficiencies and other hematopoietic-related disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bone marrow indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of

hematopoietic and immune disorders, which include, but are not limited to the following: leukemias, lymphomas, auto-immunities, immunodeficiencies (e.g. AIDS), immuno-suppressive conditions (transplantation) and other hematopoietic disorders, such as multiple myeloma. In addition this gene product may be applicable in conditions of general microbial infection, inflammation or cancer. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:88 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 694 of SEQ ID NO:88, b is an integer of 15 to 708, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:88, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 79

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

SQIKSEKKHIGKAYTCTQTQSTGMQSTLTIVAKKKSRNHTESYTRKKQENQIV
LIPWHQKKHPEGTHTCSHSLRRDTNTAADTQRKIRAHRYTYRRDKYSDTLVTH
DHYKGDKHPSNTHTQPR XEFLQPGGSTNSRAAAPRXSSSFCPFS EGYS
SWGYPH (SEQ ID NO:404), GMQSTLTIVAKKKSRNHTESYTRKKQ (SEQ ID
NO:405), KKHPEGTHTCSHSLRRDTNTAADT (SEQ ID NO:406), and/or RRDKY
SDTLVTHDHYKGDKHPSNT (SEQ ID NO:407). Polynucleotides encoding these
polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as leukemias, lymphomas, AIDS, arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification

of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:238 as residues: Asp-38 to Leu-43.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including leukemias, lymphomas, AIDS, arthritis and asthma, as well as other conditions which potentially implicate the immune system, such as atherosclerosis, cancer and infection. In addition, This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosus, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:89 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 935 of SEQ ID NO:89, b is an integer of 15 to 949, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.

5

FEATURES OF PROTEIN ENCODED BY GENE NO: 80

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KHLPLKAPIDLDNKNSCMFCSRDIKCRFH HSTAWLFL GRITDRILGLHHYLIRYQFEIENLCLMKIVIPVSMKTNCQDFDLGQLKQNL YH (SEQ ID NO:408), APIDLDNKNSCMFCSRDIKCR (SEQ ID NO:410), and/or IENLCLMKIVIPVSMKTNCQDFDLGQL (SEQ ID NO:409). Polynucleotides encoding these polypeptides are also encompassed by the invention.

15 This gene is expressed primarily in prostate carcinoma cell line stimulated with 30 nM synthetic androgen, R1881 cells and, to a lesser extent, in activated monocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive or immune disorders, particularly prostate cancer and prostate ailments. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the prostate indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and intervention of prostate cancer and prostate ailments, or related proliferative conditions in either said tissue or other tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:90 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1157 of SEQ ID NO:90, b is an integer of 15 to 1171, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 81

The translation product of this gene shares strong sequence homology with human protocadherin 42 (GenBank accession no. gil387675), PCDH7 (BH-Pcdh)a, and its associated isoforms PCDH7 (BH-Pcdh)b, and PCDH7 (BH-Pcdh)c which are thought to be important in tissue and cell-cell adhesion, repair and development (See Genbank Accession Nos.gnllPIDld1026122 (AB006755), gnllPIDld1026123 (AB006756), and gnllPIDld1026124 (AB006757)). The polynucleotides encoding this gene have been gened by another group subsequent to our filing (See Yoshida K, et al. Genomics 1998 May 1;49(3):458-61, which is hereby incorporated by reference). The cytoplasmic domain of cadherin interacts with the cytoskeleton through catenins and other cytoskeleton associated proteins. The cytoplasmic domain is not present in all cadherins, but in those which possess it, it is essential for the cadherins adhesive function. The cadherins which do not possess a cytoplasmic domain appear to function via a different method from those with a cytoplasmic domain. This protein sequence is involved in cell-cell adhesion. This sequence may have regulatory functions in the cell, as well as the cell-cell adhesive properties. Antibodies produced against this sequence are useful for modulating the binding activity of protocadherins, and can be used therapeutically. BH-Pcdh has an extracellular domain consisting of seven repeats of the cadherin motif (EC 1 to 7). EC2 of BH-Pcdh is unique in having a 55-amino-acid insertion in the middle of the motif. There are three isoforms of BH-Pcdh, denoted -a, -b, and -c, which have different cytoplasmic tails and a 47-amino-acid deletion in the EC2-3 region of BH-Pcdh-c. While only a 9.0-kb message was detected in normal tissues, 4.5- and 9.0-kb mRNA species were seen in the human lung carcinoma cell line A549. Furthermore, only the 4.5-kb mRNA was detected in HeLa cell S3 and

human gastric cancer cell lines MKN28 and KATO-III. Southern blot analysis indicated that the BH-Pcdh gene is likely to be conserved among various vertebrates. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

- 5 GTSVNESVSNATAIDSQIARSLHIPLTQDIAGDPSYEISKQRLSIVIGVVAGI (SEQ ID NO:411), PKIKMAMKPAKKITKTFLHPNSMTNLKSLKRTRKTKNLSSLSTA
ALSLWRLLSQMDRGMIVSMRSCQTAQ AWGDTGPLMVGPVAVLTWQGITNL
VPHCLLFSFIPSHQLQEKNTRPYKIYHQPTHLWEQETTFQLDQITAL STAVKP
10 ITSTANRCVYIHTLLCLAEFHSNMMLHYAPYCDDLSTPKPAGACPWPWGVVSQS
LLVPLVVFHIF ESFSFSYTEK (SEQ ID NO:412), CSIMHHTVMTFLLRNLLEPA
LGRGVSANHCLFHLLYLFL SLFLSHIQKNSMKIK (SEQ ID NO:413), TAIDS
QIARSLHIPLTQDIAGDPSYEISK (SEQ ID NO:414), YCRSKNKNNGYEAGKKDH
EDFF (SEQ ID NO:415), GPGSPDLARHYKSSSPLPTVQ (SEQ ID NO:416), and/or
15 LPPANTFVGAGDNISIGSDHCSEYS (SEQ ID NO:417). Polynucleotides encoding
these polypeptides are also encompassed by the invention. The gene encoding the
disclosed cDNA is believed to reside on chromosome 4. Accordingly, polynucleotides
related to this invention are useful as a marker in linkage analysis for chromosome 4.

This gene is expressed primarily in ovarian tumors, and to a lesser extent in, striatum and HL-60 cells.

- 20 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and reproductive dysfunction, in addition to cardiovascular and neural disorders, such as atherosclerosis, and neurodegenerative disorders, such as
25 Alzheimer's and Parkinson's, or other disorders resulting from aberrant cell-adhesion. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive, nervous and immune systems, expression of this gene at significantly
30 higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, neural, cardiovascular, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an
35 individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:240 as residues: Tyr-15 to Leu-59, Ala-68 to Asp-85, Pro-87 to Asn-96, His-120 to Lys-129, Ser-153 to Gln-170.

The tissue distribution in ovarian and muscle tissue, combined with the strong
5 homology to various cadherins indicates that polynucleotides and polypeptides
corresponding to this gene are useful for the diagnosis, study and treatment of various
neoplastic disorders such as squamous cell carcinomas and related tumors, and nervous
system and reproductive disorders. Considering the vital importance of cell-adhesion
amongst various cellular functions, in particular chemotaxis by the immune and
10 hematopoietic cells indicates that this gene product may play a direct, or in-direct role in
the regulation of cytokine production, antigen presentation, or other processes that may
also suggest a usefulness in the treatment of cancer (e.g. by boosting immune
responses). Since the gene is expressed in cells of lymphoid origin, the natural gene
product may be involved in immune functions. Therefore it may be also used as an
15 agent for immunological disorders including arthritis, asthma, immunodeficiency
diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease,
inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis,
hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to
transplanted organs and tissues, such as host-versus-graft and graft-versus-host
20 diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue
injury, demyelination, systemic lupus erythematosus, drug induced hemolytic anemia,
rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene
product may have commercial utility in the expansion of stem cells and committed
progenitors of various blood lineages, and in the differentiation and/or proliferation of
25 various cell types. Furthermore, the secreted protein can also be used to determine
biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or
receptors, to identify agents that modulate their interactions and as nutritional
supplements. It may also play an in-direct role in the regulation of a very wide range of
biological activities. Typical of these are cytokine, cell proliferation/differentiation
30 modulating activity or induction of other cytokines;
immunostimulating/immunosuppressant activities (e.g. for treating human
immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation
of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation
or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating
35 wounds, stimulation of follicle stimulating hormone (for control of fertility);
chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic
or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-

inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against
 5 the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:91 and may have been publicly available prior to conception of the present
 10 invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1137 of SEQ ID NO:91, b is an integer of 15
 15 to 1151, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 82

20

The translation product of this gene shares sequence homology with the G-protein coupled receptor TM3 consensus polypeptide which may implicate an important function for this protein in various signal transduction pathways. G-protein coupled receptors are known to have a variety of functions including modulating immune
 25 system tissue through interaction with cytokines and lymphokines. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

GTSNASVSPTICICMCGYVHIWFFICLCVYLKVLQGSACPWIAAAVVMRRMRK
 VQEKGEVFRNMAATWAL RSGIQSLNSLVSSAFFTIFMTLGSSWNLIVSLSSLV
 30 NWTGLFSFYFSRN (SEQ ID NO:418), CLCVYLKVLQGSACPWIAAAV
 MRRMRK (SEQ ID NO:419), and/or TIFMTLGSSWNLIVSLSSLVNWTGLF (SEQ ID NO:420). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in breast lymph node.

35 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, breast cancer, or other immune or reproductive disorders and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, reproductive, breast, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, breast milk, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:241 as residues: Cys-34 to Gly-48.

The tissue distribution in breast lymph nodes and homology to a conserved G-protein coupled receptor TM3 consensus sequence indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment for breast cancer or immune diseases. Considering the vast roles which G-protein coupled receptors play in the maintenance of important cellular functions, the secreted protein may have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Furthermore, the protein may also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:92 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more

- 5 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 700 of SEQ ID NO:92, b is an integer of 15 to 714, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.

10

FEATURES OF PROTEIN ENCODED BY GENE NO: 83

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

- 15 QPDIPVLPVGFSQLNCSFKVSGCWKGGGLIAEKVGTLGTPKGRR AWPETEF
FRFLEPGLP (SEQ ID NO:421), and/or RGFRMAQPLVNTFQVAVPVEDL
APQQNPSRFPADPALLSFLTG SILAPGKVIWVNVSTAIWPTWDSMAI
GELTIASHASMTLHIGRPGSRKRKNSVSGHARLPFGVPSVPT FSAISPP
FQQPETLKEQF (SEQ ID NO:422). EDLAPQQNPSRFPADPALLSFLTG (SEQ ID
20 NO:423), and/or TWDSMAIGELTIASHASMTLHIGRPGSRK (SEQ ID NO:424).
Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in activated T-cells, hepatocellular tumor, pancreas islet cell tumors, and hemangiopericytoma.

- 25 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hepatic, and endocrine disorders, such as cancers, particularly of T-cells, hepatocellular tumors and pancreas islet cell tumors. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological
30 probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hepatic, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or
35 another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:242 as residues: Glu-43 to Lys-50, Ser-53 to Phe-60.

5 The tissue distribution in T-cells, hepatocellular tumors, and pancreatic islet cell tumors indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of immune, hepatic, and endocrine disorders, and other cancer types. Expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders in various tissues, aside from those disclosed above. Similarly, developmental tissues rely
10 on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

15 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:93 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.
20 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 796 of SEQ ID NO:93, b is an integer of 15 to 810, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or equal to a + 14.

25

FEATURES OF PROTEIN ENCODED BY GENE NO: 84

30 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
VSPQLMGIKREPSAAQLSVGEEHTLDREGRELVDLPGQPSQKIKIKNKSSLHPG
LIIPP AHYKTATTTNLF (SEQ ID NO:425), and/or PSAAQLSVGEEHTLDREGREL
(SEQ ID NO:426). Polynucleotides encoding these polypeptides are also encompassed by the invention.

35 This gene is expressed primarily in hepatocellular tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic disorders, such as liver diseases and hepatocellular tumor, including proliferative disorders in other tissues and cell types. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. hepatic, proliferating, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hepatocellular tumor tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of hepatocellular tumor or other liver disorders. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:94 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1162 of SEQ ID NO:94, b is an integer of 15 to 1176, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:94, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 85

When tested against reh cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is

likely that this gene activates B-cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells.

- 5 Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: NCDHDFIQPLHTPMSAL FQSEFS (SEQ ID NO:427), SILNM GLFTEQRPWPAAARCARQSTVAGAIRRARGTVTMWQVAGAAW ASPDRRAKV
- 10 HPCRHAAPCLPSPCRRGLQMSGPLQATRGRVTLRSHQVGCKRATGSIENSL (SEQ ID NO:428), QKSKGSPLQTCCSLPTLPMQERPADEWSTPGDQGKSYIK KPPGGLQKGHRLHRKLTLKQGRHRGVE GLNEIMVTVLKEEFPVSKPGLNV LPTFHRHHECYQHGMNLTARISVVS (SEQ ID NO:429), ARQSTVAGAIRR ARGTVTMWQVAGA (SEQ ID NO:430), PCRRGLQMSGPLQATRGRVTLRSHQ
- 15 (SEQ ID NO:431), LPMQERPADEWSTPGDQGKSYIKKPP (SEQ ID NO:432), and/or NVLPTFHRHHECYQHGMNLTARI (SEQ ID NO:433). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human fetal kidney, adult testis, T-cell lymphoma, and a fetal liver/spleen cDNA library.

- 20 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal, developmental, reproductive, immune, or hematopoietic disorders, particularly kidney disease, lymphoma, congenital defects, multiple myeloma, SCID,
- 25 male sterility, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the kidney and immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune,
- 30 hematopoietic, reproductive, renal, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 35 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:244 as residues: Gly-35 to Gly-40.

The tissue distribution in fetal kidney and T-cells, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis or treatment of kidney diseases or immune disorders, especially cancers. Specifically, this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:95 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1014 of SEQ ID NO:95, b is an integer of 15 to 1028, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:95, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 86

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells.

Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

5 This gene is expressed primarily in breast, human embryo, and chronic spleen lymphocytic leukemia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, developmental, hematopoietic or immune disorders, such as breast cancer, congenital birth defects, or leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast or hematopoietic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, immune, hematopoietic, developmental, breast, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, breast milk, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:245 as residues: His-2 to Asn-8, Gln-35 to Phe-44.

The tissue distribution in breast and lymphocytic leukemia cells, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis or intervention of breast cancer, leukemia or other hematopoietic related disorders. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies

directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:96 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 733 of SEQ ID NO:96, b is an integer of 15 to 747, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:96, and where b is greater than or equal to a + 14.

15 FEATURES OF PROTEIN ENCODED BY GENE NO: 87

This gene is expressed primarily in brain containing medulla blastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly specific brain tumors such as medulla blastoma, as well as other diseases and conditions of the brain, such as schizophrenia, Alzheimer's disease, Tourette's syndrome, Parkinson's disease, Huntington's disease, mania, dementia, paranoia, depressive and addictive predispositions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of specific brain tumors such as medulla blastoma. In addition it may also be useful for the diagnosis and treatment of developmental, degenerative and behavioral conditions of the

brain and nervous system, such as schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, Tourette's syndrome, mania, dementia, paranoia, addictive behavior, obsessive-compulsive and sleep disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:97 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 614 of SEQ ID NO:97, b is an integer of 15 to 628, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:97, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 88

When tested against Jurket cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates T-cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: INVLYCSRDSL MGRTIMESSDYIKKGANVSPVLGVRQQ AV (SEQ ID NO:434). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in adrenal gland tumor and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the endocrine and immune or haemopoietic systems, particularly inflammatory or immunodeficiency conditions, such as AIDS. Similarly,

polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and endocrine systems, expression of this gene at significantly higher or lower levels may
5 be detected in certain tissues or cell types (e.g. immune, hematopoietic, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the
10 disorder.

The tissue distribution in T-cells and adrenal gland tissues, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the immune and endocrine systems and cancer. Moreover, the secreted protein can also be
15 used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for
20 treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections,
25 tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies
30 directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:98 and may have been publicly available prior to conception of the present
35 invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 890 of SEQ ID NO:98, b is an integer of 15 to 904, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:98, and where b is greater than or equal to a + 14.

5

FEATURES OF PROTEIN ENCODED BY GENE NO: 89

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: SLLMYFVFKIFFQSLCVLGYCILPLTVA (SEQ ID NO:435). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:248 as residues: Thr-43 to Thr-48.

The tissue distribution in dendritic cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of immune system disorders. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product

may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

- 5 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:99 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.
- 10 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 562 of SEQ ID NO:99, b is an integer of 15 to 576, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:99, and where b is greater than or equal to a + 14.

15

FEATURES OF PROTEIN ENCODED BY GENE NO: 90

- 20 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
RLWMTKAHPALRHLLLLFTLALTLLAQGCCAVAPSGCADLAGFCSLGHS C
(SEQ ID NO:436). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human stomach.

- 25 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, digestive and gastrointestinal conditions, particularly ulcers and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in
- 30 providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the gastrointestinal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.gastrointestinal, metabolic, mucosal, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, chyme,
- 35 plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression

level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:249 as residues: Pro-32 to Gly-38.

5 The tissue distribution in stomach tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study and treatment of gastrointestinal disorders, or other disorders afflicting mucosal or endothelial tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

10 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:100 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

15 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 699 of SEQ ID NO:100, b is an integer of 15 to 713, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:100, and where b is greater than or equal to a + 14.

20

FEATURES OF PROTEIN ENCODED BY GENE NO: 91

25 The translation product of this gene was found to have homology to the conserved K07F5.14 protein from *Caenorhabditis elegans* (See Genbank Accession No gnllPIDle233697) which may be important in regulation of important cellular functions, including homeostasis and cell division. When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) pathway. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

35 RTCTPWMGFWCLVCSLFAPVPTSRKYLVSKEPGCYQRRRV FGVCFTKPL (SEQ

ID NO:437), WLLSEKKG (SEQ ID NO:438), and/or GVFYKAAVIG (SEQ ID NO:439). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in bone marrow and T cells.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly multiple myeloma, immunodeficiencies, and cancers. Similarly, polypeptides and antibodies directed to
10 these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily
15 fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bone marrow and T-cells, combined with the detected
20 GAS biological activity in U937 cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of immune and hormonal disorders and neoplasias. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal
25 cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product
30 may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Moreover, the protein may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne,
35 neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune

infertility, lense tissue injury, demyelination, systemic lupus erythematosus, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the

5 differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

10 ID NO:101 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

15 a-b, where a is any integer between 1 to 635 of SEQ ID NO:101. b is an integer of 15 to 649, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:101, and where b is greater than or equal to a + 14.

20 FEATURES OF PROTEIN ENCODED BY GENE NO: 92

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

CKTSPLPKEGQSAVSVPVSSHFLAHSAPLSGGHAHV FARDGATGL (SEQ ID

25 NO:440), LGRGSGERKTPVSCFAQISKSRGGRSKSLTHLCTHTHTQVTEL
DVRMSHGCLR XQHAGRLAPPPPLRFCL TACWGRRGEAETVWKDPASSQ
HPPPSEKPHRQDRHPERWHQPGGPIPGKHMRVSPGQRGRVCQEMGRNRN
(SEQ ID NO:441), FCLRDFKIWRGRLEAGRTEGRL AGERFGGEEDPSFLFC
SDFKVEGWAFEISHSLVHTHTHTGHGAGRADVTRVPAGTARWEAGSPTPSPV

30 LF DSLLGAAGRG (SEQ ID NO:442), AQISKSRGGRSKSLTHLCTHTHTQVTEL
(SEQ ID NO:443), EKPHRQDRHPERWHQPGGPIPGKHMR (SEQ ID NO:444),
GRLEAGRTEGRL AGERFGGEEDPSFL (SEQ ID NO:445), and/or
VTRVPAGTARWEAGSPTPSPVLF (SEQ ID NO:446). Polynucleotides encoding
these polypeptides are also encompassed by the invention. The gene encoding the

35 disclosed cDNA is believed to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in ovary, spinal cord, and fetal spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, reproductive, and neurological conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developmental, reproductive, ovarian, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:251 as residues: Pro-34 to Pro-53.

The tissue distribution in spinal cord and fetal spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study and treatment of neural, hematopoietic, and developmental disorders. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia,

leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include, but are not limited to bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:102 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 683 of SEQ ID NO:102, b is an integer of 15 to 697, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:102, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 93

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: DEGVQGERLFRILRINGEKPYNFVDYFHCEY (SEQ ID NO:447), KVVRIIDNGILCSHKKTEIMSLQQHGWWRPYLKQNTGTENQIPHTL TYKWELNFEYIXTQXRGXXDSEAYLKVEGGRREGIQKLPIRYVYYLGDKIICT SSSCSMHLLM (SEQ ID NO:448), HKDTCMSMFT AALFTIAKTWN (SEQ ID NO:449), MPINDRLDFKRWYV (SEQ ID NO:450), TMESYVAIKRQRSCPCSNM VGSGGHILSKLTQEQTKEYHILS LISGS (SEQ ID NO:451), EIMSLQQHGWWR PYLKQNTGTEN (SEQ ID NO:452), and/or RREGIQKLPIRYVYYLGDKIICT (SEQ ID NO:453). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in bladder tissue from a human male.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal, urogenital, and nephrotic conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a

number of disorders of the above tissues or cells, particularly of the gastrointestinal and excretory systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. renal, bladder, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:252 as residues: Arg-52 to Ala-57, Pro-66 to Thr-72.

The tissue distribution in bladder tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of gastrointestinal and urinary tract disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:103 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1274 of SEQ ID NO:103, b is an integer of 15 to 1288, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:103, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 94

This gene is expressed primarily in bladder tissue from a human male.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal, renal, and urinary tract conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the intestinal and urinary tract, expression of this gene at significantly higher or lower levels may be

detected in certain tissues or cell types (e.g. renal, urogenital, bladder, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bladder tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of urinary tract and gastrointestinal disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:104 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1013 of SEQ ID NO:104, b is an integer of 15 to 1027, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:104, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 95

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LHGEQVPI YIFLLMQPLNFECISFLNCIEQYSVGVI HNSV TIYACDREENCMDIRYL (SEQ ID NO:454), and/or GTSWASRFFTC (SEQ ID NO:455). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and inflammatory disorders, particularly immunodeficiencies such as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of

the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:254 as residues: Lys-28 to Thr-34.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the immune system. Moreover, This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosus, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:105 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 696 of SEQ ID NO:105, b is an integer of 15 to 710, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:105, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 96

5 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

GPPRXFXPKKAILGXPPXGRVPPFRYRSRNSRGRPHXSAPRVRFCLNSWLR
(SEQ ID NO:456), and/or PLNTMMCMCKMKVSPKIFSKLKRKYLSNTLTKL
EMQTVHLESSLASCSPNKGXVGRTR GVDPGNSGTGT (SEQ ID NO:457).

10 Polynucleotides encoding these polypeptides are also encompassed by the invention.

 This gene is expressed primarily in lymphoma and frontal cortex.

 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological and haemopoietic diseases, particularly neurodegenerative conditions such as Alzheimers and Parkinsons. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and neural systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

 The tissue distribution in frontal cortex and lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases of the neural and haemopoietic systems. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this

gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Moreover, the expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Since, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:106 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 516 of SEQ ID NO:106, b is an integer of 15 to 530, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:106, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 97

This gene is expressed primarily in the spleen of a patient with metastatic melanoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly metastatic melanoma and other cancers, as well as immune disorders and conditions such as anemias, AIDS.

arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or
5 lower levels may be detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an
10 individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:256 as residues: Pro-26 to Asn-34.

The tissue distribution in spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of metastatic
15 melanomas and other cancers, as well as other immune disorders and conditions including leukemias, lymphomas, AIDS, arthritis, asthma and microbial infection. Furthermore, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, or thrombocytopenia since stromal cells are important in the
20 production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the
25 expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available
30 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:107 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more
35 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 378 of SEQ ID NO:107, b is an integer of 15

to 392, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:107, and where b is greater than or equal to a + 14.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 98

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GTVTQKRK CVFGKYLLSTCSLMFSSMHGACSWKA KQTSSSAGFLCLHVLCPALQLTREKYKTWPWPSFI (SEQ ID NO:458), and/or
10 MKEGQGHVLYF SRVNCKAGHXTCRQRKPADELVCFAFQEQA PCILLNI RLQVLNKYLPNTHFLFCVTVP (SEQ ID NO:459). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

15 This gene is expressed primarily in pineal gland and synovial sarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine or skeletal disorders, including cancers. Similarly,
20 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. endocrine, pineal, skeletal, and cancerous and wounded
25 tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in pineal gland indicates that polynucleotides and
30 polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the endocrine system. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancreas (e.g. diabetes mellitus),
35 adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-, hypoparathyroidism), hypothalamus, and testes. Alternatively, the expression of this gene product in synovium would suggest a

role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chondromalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders
5 such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or
10 immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:108 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the
15 scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 977 of SEQ ID NO:108, b is an integer of 15 to 991, where both a and b correspond to the positions of nucleotide residues shown in
20 SEQ ID NO:108, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 99

25 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

TMTGIDSSPEEILRQVGCKQQGKGVEHVEGSSAEAGEAARGGGAK GGGG
AAGKGTSKVGTLRRTRGST (SEQ ID NO:460). Polynucleotides encoding these polypeptides are also encompassed by the invention.

30 This gene is expressed primarily in breast and fetal spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the reproductive system and developing organs, particularly
35 congenital defects afflicting the immune or hematopoietic system, such as immunodeficiencies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification

of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, developing, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:258 as residues: Gly-23 to Asn-30. Ser-37 to Asn-43.

The tissue distribution in fetal spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases involving developmental tissues and reproductive organs. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:109 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 898 of SEQ ID NO:109, b is an integer of 15 to 912, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:109, and where b is greater than or equal to a + 14.

5

FEATURES OF PROTEIN ENCODED BY GENE NO: 100

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

10 AQREAGSRPRRRKSLKAVAMXLXVEMGGGCRGSMGPGPGYSAGSRVCRGSSL
PQVAPFNPSRAHLLPPVVG GGLNSVWLSGVQLSTPPYADWEGVGQSPQ
PRGPWMGSSSLGTVGPGCVLSGCPTVKANGGSPCSEMLGER RLLEPSVG
PVSGCPERREGGHGARGAAGVVVKGHASVQLNFLSLI (SEQ ID NO:461).
KAEFTFAKEKNAKAQLGKKGTRWVKHDKRKEIQLYGCVTLNDDPSCPPCPVP
15 TLPPFWTA TYGSHGRFQKPPFSQHLRAGGAPVGLDCGAPTQYAARPHGPK
(SEQ ID NO:462), GCRGSMGPGPGYSAGSRVCRGSSLPQ (SEQ ID NO:463),
QPRGPWMGSSSLGTVGPGCVLS (SEQ ID NO:464), and/or GAAGVVVKGH
ASVQLNFLSLI (SEQ ID NO:465). Polynucleotides encoding these polypeptides are
also encompassed by the invention.

20 This gene is expressed primarily in endothelial, immune, and cancer cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases involving immune, endothelial, and haemopoietic tissues or
25 cells, particularly cancers, inflammatory or immunodeficiency conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, haemopoietic and endothelial systems, expression of this gene at significantly higher or
30 lower levels may be detected in certain tissues or cell types (e.g. endothelial, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an
35 individual not having the disorder.

The tissue distribution in immune and hematopoietic tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis

and treatment of disorders of the immune and haemopoietic systems, including cancer. More specifically, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosus, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO: 110 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 861 of SEQ ID NO: 110, b is an integer of 15 to 875, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 110, and where b is greater than or equal to a + 14.

30

FEATURES OF PROTEIN ENCODED BY GENE NO: 101

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GKPLSAIFPICH MMFLPGKFNLGISHRCCRMT SPWDK RQQLRQECKSDPHVQNPRIHFPESKNSFPSAYIFVSEGNGVSPSK WHCIY SGTSLSH (SEQ ID NO: 466), and/or GERGRYQSKYSATWMVTPHYLQTQRC

35

KLREMNSWIQGNFLDSEHEGQIYIPVSIVDAYPKD (SEQ ID NO:467).

Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human kidney, and to a lesser extent, in liver.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, kidney, urogenital, hepatic, and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing
10 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal or endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. urogenital, kidney, endocrine, hepatic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, bile,
15 urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID
20 NO:260 as residues: Glu-38 to Lys-43.

The tissue distribution in kidney indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of renal disorders, including noninflammatory and inflammatory lesions, and tumors of the kidney. Moreover, this gene or gene product could be used in the treatment and/or detection of
25 kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Alternatively, expression within liver
30 indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets
35 for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:111 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more
5 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 445 of SEQ ID NO:111, b is an integer of 15 to 459, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:111, and where b is greater than or equal to a + 14.

10

FEATURES OF PROTEIN ENCODED BY GENE NO: 102

This gene is expressed primarily in kidney cortex and fetal tissue.utility_

The tissue distribution in kidney indicates that this gene or gene product could
15 be used in the treatment and/or detection of kidney diseases including renal failure, nephritis, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's
20 syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:112 and may have been publicly available prior to conception of the present
25 invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 595 of SEQ ID NO:112, b is an integer of 15
30 to 609, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:112, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 103

35

This gene is expressed primarily in ovary and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive and neurological conditions, particularly proliferative disorders, such as ovarian cysts or cancer, in addition to neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, reproductive, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in ovarian tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of reproductive disorders, such as infertility. Alternatively, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:113 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1390 of SEQ ID NO:113, b is an integer of 15 to 1404, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:113, and where b is greater than or equal to a + 14.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 104

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ISIRGRIL

YKMAYFKVCVIIWFQQFCVEETSIKKNVRMLTSEFQNSYATPVSGLLPGAVAWR
 15 GGAVYGWVRHAMQVLQ KEPTQPSSFLPPSDAASFSGPESRLHLTW (SEQ ID
 NO:468), KPFAFSARNFPTMLSEAYFQDPRMRQHHLGVERMTV AWVPSAIP
 AWRASPTRTQHHPKPKQHQEGAQKQGWMMNSGILMSAYEHFL (SEQ ID
 NO:469), and/or HSKQNICREVNILKMFLHEIKKTVTDNISTQRRFTYNHQP
 20 VSIFSVDILDFEVPFGL (SEQ ID NO:470). Polynucleotides encoding these
 polypeptides are also encompassed by the invention.

This gene is expressed primarily in melanocytes, and PHA stimulated T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or integumentary system disorders, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain
 25 tissues or cell types (e.g.integumentary, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

35 The tissue distribution in immune cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of cancers and immune system disorders. Alternatively, the expression in melanocytes

indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athlete's foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chondromalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:114 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 839 of SEQ ID NO:114, b is an integer of 15 to 853, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:114, and where b is greater than or equal to a + 14.

35 FEATURES OF PROTEIN ENCODED BY GENE NO: 105

This gene is expressed primarily in B cell lymphoma, and to a lesser extent, in dermal fibrosarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or integumentary disorders, particularly lymphatic and soft tissue cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in B-cell lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the protein product of this gene may also be useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to

viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athletes foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chondromalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:115 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 831 of SEQ ID NO:115. b is an integer of 15 to 845, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:115, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 106

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

KVIDVIFSLPPGRKATFSCPLAPLSGAXGLPGGGANRPGPFLPCIQPWGPLRLP
EGC (SEQ ID NO:471), MSSSLCPQGGKPPSLAPWPLCQGPXVCRVGVPT

GLALSSPASSHGGLCDCRKVAWLVPGPAQARG RAAWFYFYLTLSVL (SEQ ID NO:472), and/or LALSSPASSHGGLCDCRKVAWLVPGP (SEQ ID NO:473).

Polynucleotides encoding these polypeptides are also encompassed by the invention.

5 This gene is expressed primarily in T cells, fetal liver, and to a lesser extent, in various normal and transformed tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, or developmental disorders, including
10 immunodeficiencies and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune,
15 hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

20 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:265 as residues: Arg-5 to Pro-12.

The tissue distribution in B-cells and fetal liver indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of immune and developmental disorders. Moreover, polynucleotides and polypeptides
25 corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of
30 neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. In addition, expression within fetal tissue and
35 other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues

rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:116 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 746 of SEQ ID NO:116, b is an integer of 15 to 760, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:116, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 107

One embodiment of this gene comprises the following amino acid sequence:
MQRERWARPWMASSTVESRMPEGKWRRFSTDLATWGATPARSWTKASRGSTT
AWTRLPMRSTMVLDKQERKQQRSLAMGSTTLLDRPGRKQTKRSKGSTLGSTRL
GRKQRNLAKGSTMLLTRLERXWRSQAQVPTMLLARPGRSCRMIMGSTKPAR
RPTSC (SEQ ID NO:474). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in keratinocytes and tissues undergoing wound healing, and to a lesser extent, in osteoblasts and smooth muscle.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skin disorders; fibrosis; scarring; osteoporosis; osteopetrosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, bone, or connective tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. skin, bone, connective tissues, cancerous and wounded tissues) or bodily fluids (e.g. lymph. serum, plasma, urine,

synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 5 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:266 as residues: Gly-76 to Leu-83, Ala-108 to Glu-113, Ala-126 to Lys-132, Gly-145 to Leu-151.

- The tissue distribution in keratinocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of skin disorders. Elevated expression of this protein in skin and keratinocytes suggest that it may be involved in keratinocyte proliferation, survival, and/or differentiation. Thus, it may play a role in such processes as fibrosis and wound healing. Similarly, expression of this protein in osteoblasts indicates that it may also play a role in osteoblast survival, proliferation, and/or differentiation, and that it may be useful in the treatment of such disorders as osteoporosis or osteopetrosis.
- 10
15

- Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:117 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 974 of SEQ ID NO:117, b is an integer of 15 to 988, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:117, and where b is greater than or equal to a + 14.
- 20
25

FEATURES OF PROTEIN ENCODED BY GENE NO: 108

- 30 The translation sequence of this gene shares homology with a mouse camodulin binding protein. The calcium-binding regulatory protein calmodulin is an essential subunit of the erythrocyte and other plasma membrane calcium ATPases. A rise in cytosolic calcium induces the binding of calcium ions to calmodulin, which triggers an allosteric activation of the calcium ATPase, and subsequently an export of calcium ions from the cell is accelerated.
- 35

This gene is expressed primarily in teratocarcinoma cells, and to a lesser extent, in myeloid progenitor cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental defects, calcium-transport defects, in addition to immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of embryonic and fetal tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developing tissues, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:267 as residues: Tyr-124 to Gly-129.

The tissue distribution in teratocarcinoma cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of developmental defects as well as for organ regeneration. Moreover, expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Alternatively, the homology of the translation product of this gene to a mouse calmodulin binding protein indicates that the translation product of this gene may be useful for disorders involving calcium transport across the plasma membrane, for example. It has further been suggested this type of disorder may be responsible for disorders such as hypertension.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:118 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1933 of SEQ ID NO:118, b is an integer of 15 to 1947, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:118, and where b is greater than or equal to a + 14.

5

FEATURES OF PROTEIN ENCODED BY GENE NO: 109

One embodiment of this gene comprises polypeptides of the following amino acid sequence:

MRPLLGLLLVFAGCTFALYLLSTRLPGRRLGSTEEAGGRSLWFPSDLAELREL
SEVLREYRKEHQAYVFLFLFCGAYLYKQGFAIPGSSFLNVLGALFGPWLGILLI
CCVLTSVGATCCYLLSSIFGKQLVVSYPDKVALLQRKVEENRNSLFFFLLFLR
LFPMTPNWFLNLSAPILNIPIVQFFFSVLIGLI PYNFICVQTGSILSTLTSLDA
LFSWDTVFKLLAIAMVALIPGTLIKFSQKHLQLNETSTANHIHSRKDT (SEQ ID
NO:475). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in ovarian tumor, and to a lesser extent, in smooth muscle and breast cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers, particularly of the ovary, musculature, and breast, such as rhabdomyosarcomas or fibroids. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. ovaries, breast, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, breast milk, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:268 as residues: Arg-24 to Arg-29.

The tissue distribution in ovarian tumor tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of

cancer, particularly ovarian and breast cancers. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available
5 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:119 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more
10 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1434 of SEQ ID NO:119, b is an integer of 15 to 1448, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:119, and where b is greater than or equal to a + 14.

15

FEATURES OF PROTEIN ENCODED BY GENE NO: 110

The translation product of this gene shares sequence homology with bovine
acrosin inhibitors IIa and IIb which is thought to be important as protease inhibitors.

20 This gene is expressed primarily in keratinocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integumentary disorders, such as psoriasis, and wound healing
25 aberrations. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the integumental system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.integumentary, and cancerous and
30 wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID
35 NO:269 as residues: Tyr-39 to Lys-58.

The tissue distribution in keratinocytes, combined with the homology to the bovine acrosin inhibitors IIa and IIb indicates that polynucleotides and polypeptides

corresponding to this gene are useful for the acceleration of wound healing. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available
5 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:120 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more
10 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 482 of SEQ ID NO:120, b is an integer of 15 to 496, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:120, and where b is greater than or equal to a + 14.

15

FEATURES OF PROTEIN ENCODED BY GENE NO: 111

This gene is expressed primarily in fetal liver/spleen, T cells, and to a lesser extent, in bone marrow and primary dendritic cells.

20 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; immune dysfunction; lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing
25 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or
30 another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:270 as residues: Glu-28 to His-34.

35 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders. This gene product is primarily expressed in hematopoietic cells

and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoietic lineages. This is particularly supported by the expression of this gene product in fetal liver and bone marrow, the two primary sites of definitive hematopoiesis. Expression of this gene product in T cells and primary
5 dendritic cells also strongly indicates a role for this protein in immune function and immune surveillance. Furthermore, since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available
10 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:121 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more
15 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1160 of SEQ ID NO:121, b is an integer of 15 to 1174, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:121, and where b is greater than or equal to a + 14.

20

FEATURES OF PROTEIN ENCODED BY GENE NO: 112

The gene encoding the disclosed cDNA is thought to reside on chromosome 14. Accordingly, polynucleotides related to this invention are useful as a marker in linkage
25 analysis for chromosome 14.

This gene is expressed primarily in fetal liver, spleen, and to a lesser extent in melanocyte.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
30 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, integumentary, or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of fetal and embryonic
35 tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, developmental, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine,

synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

5 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:271 as residues: Met-1 to Met-7, Gln-43 to Glu-50, Thr-89 to Thr-95.

The tissue distribution in fetal liver and spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of developmental hematopoietic disorders. Additionally, the tissue distribution indicates
10 that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders. This gene product is primarily expressed in hematopoietic cells and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoietic lineages. This is particularly supported by the expression of this gene product in fetal liver, which is a
15 primary sites of definitive hematopoiesis, and strongly suggesting a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:122 and may have been publicly available prior to conception of the present
20 invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID NO:122, b is an integer of 15
25 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:122, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 113

30 When tested against Jurkat T-cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates T-cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are
35 involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS

element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in B cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as
5 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, B cell lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential
10 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e.,
15 the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:272 as residues: Gln-23 to Asn-31, Tyr-42 to Ser-58.

The tissue distribution in B-cells indicates that polynucleotides and polypeptides
20 corresponding to this gene are useful for treatment and diagnosis of lymphomas, particularly B cell lymphomas. Furthermore, expression of this gene product in B-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen
25 presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders
30 including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the
35 protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Additionally, the biological activity data supports the notion that the

translational product of this gene activates specific immune cells, and therefore may play a role in the initiation of immune system activity.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:123 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1146 of SEQ ID NO:123, b is an integer of 15 to 1160, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:123, and where b is greater than or equal to a + 14.

15 FEATURES OF PROTEIN ENCODED BY GENE NO: 114

This gene is expressed primarily in neutrophils: IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of certain immune disorders, especially those involving neutrophils. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a

usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for

5 immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies

10 directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:124 and may have been publicly available prior to conception of the present

15 invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 879 of SEQ ID NO:124, b is an integer of 15

20 to 893, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:124, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 115

25

One embodiment of this gene comprises polypeptides of the following amino acid sequence: DIMPASVIFLICEGVLYGVQG (SEQ ID NO:476). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in placenta.

30

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, placental insufficiency; developmental abnormalities; aberrant angiogenesis; abnormal development and/or maintenance of the placenta. Similarly,

35 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the placenta and, more

generally, the vasculature and/or endothelium, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developing, placental, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in placental tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:125 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1035 of SEQ ID NO:125, b is an integer of 15 to 1049, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:125, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 116

This gene is expressed primarily in keratinocytes, as well as in synovial hypoxia and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integumentary, immune, or skeletal disorders, particularly wound healing and rheumatoid conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the integumentary system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. skin, connective tissues, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:275 as residues: Thr-42 to Pro-53, Val-78 to Glu-86, Glu-103 to Met-112, Ala-124 to Gly-131.

The tissue distribution in keratinocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of integumentary disorders, particularly with regard to wound healing. Furthermore, the tissue distribution also indicates that the translation product of this gene is useful for the treatment and/or detection of disorders of the connective tissues (e.g. arthritis, trauma, tendonitis, chondromalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:126 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 1612 of SEQ ID NO:126, b is an integer of 15 to 1626, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:126, and where b is greater than or equal to a + 14.

5

FEATURES OF PROTEIN ENCODED BY GENE NO: 117

This gene is expressed primarily in hepatoma and testes tumor, and to a lesser extent, in brain.

10 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic, neural, or reproductive disorders, particularly metastatic liver cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful
15 in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cancer and metabolic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. liver, brain, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, seminal fluid,
20 amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hepatic tissue indicates that polynucleotides and
25 polypeptides corresponding to this gene are useful for diagnosis and treatment of some types of cancer including hepatoma, testes tumor and related metastases. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are
30 attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ
35 ID NO:127 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1163 of SEQ ID NO:127, b is an integer of 15 to 1177, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:127, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 118

10 This gene is expressed primarily in CD34 positive cells, and to a lesser extent, in pancreatic tumor and spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, endocrine, or immune disorders, particularly pancreatic cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the tumor, immune and metabolic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, liver, spleen, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, bile, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in pancreatic and CD34 positive cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some types of cancer, especially those involving CD34 cells and pancreatic cancer. Furthermore, expression of this gene product in both CD34 positive cells and spleen indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for

immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, z, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the
5 differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ
10 ID NO:128 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of
15 a-b, where a is any integer between 1 to 1262 of SEQ ID NO:128, b is an integer of 15 to 1276, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:128, and where b is greater than or equal to a + 14.

20 FEATURES OF PROTEIN ENCODED BY GENE NO: 119

This gene is expressed primarily in osteoclastoma, fetal liver/spleen, and to a lesser extent, in primary dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as
25 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteoclastoma; hematopoietic disorders; lymphomas; impaired immunity; immune disorders; inflammation, in addition to integumentary disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing
30 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and bone, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, bone, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, amniotic fluid, plasma, urine,
35 synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the

expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:278 as residues: Thr-23 to Pro-29, Thr-68 to Pro-76.

5 The tissue distribution in dendritic cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of bone and hematopoietic disorders. Elevated levels of expression of this gene product in osteoclastoma indicates that it may play a role in the survival, proliferation, and/or growth of osteoclasts. Therefore, it may be useful in influencing bone mass in such
10 conditions as osteoporosis. More generally, as evidenced by expression in fetal liver/spleen, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the numbers of stem cells and committed progenitors. Expression of this gene product in primary dendritic cells also indicates that it may play a role in mediating responses to
15 infection and controlling immunological responses, such as those that occur during immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:129 and may have been publicly available prior to conception of the present
20 invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1320 of SEQ ID NO:129. b is an integer of 15
25 to 1334, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 120

30 When tested against fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 assay. Thus, it is likely that this gene activates fibroblast cells through a signal transduction pathway. Early growth response 1 (EGR1) is a promoter associated with certain genes that induces various tissues and cell
35 types upon activation, leading the cells to undergo differentiation and proliferation.

This gene is expressed primarily in hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, soft tissue cancers, such as hemangiopericytoma, in addition to other proliferative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. circulatory system, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:279 as residues: Pro-49 to Thr-64.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of hemangiopericytoma. Furthermore, the biological activity data demonstrates that the translation product of this gene activates fibroblast cells. Fibroblast cells have the ability to undergo vascularization, and thus the translation product of this gene may be involved in disorders of the vascular tissue, such as hemangiopericytoma.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:130 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of $a-b$, where a is any integer between 1 to 518 of SEQ ID NO:130, b is an integer of 15 to 532, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to $a + 14$.

FEATURES OF PROTEIN ENCODED BY GENE NO: 121

This gene is expressed primarily in kidney cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal or urogenital disorders, particularly nephritis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. kidney, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:280 as residues: Pro-33 to Ser-38.

The tissue distribution in kidney cortex indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the kidney, including nephritis. Furthermore, the tissue distribution in kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:131 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 671 of SEQ ID NO:131, b is an integer of 15 to 685, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 122

5 This gene is expressed primarily in spleen from chronic lymphocytic leukemia.

 Therefore, polynucleotides and polypeptides of the invention are useful as
reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, immune or hematopoietic disorders, such as chronic lymphocytic
10 leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are
useful in providing immunological probes for differential identification of the tissue(s)
or cell type(s). For a number of disorders of the above tissues or cells, particularly of
the immune system, expression of this gene at significantly higher or lower levels may
be detected in certain tissues or cell types (e.g. spleen, cancerous and wounded tissues)
15 or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or
another tissue or cell sample taken from an individual having such a disorder, relative to
the standard gene expression level, i.e., the expression level in healthy tissue or bodily
fluid from an individual not having the disorder.

 The tissue distribution in spleen tissue indicates that polynucleotides and
20 polypeptides corresponding to this gene are useful for diagnosis and treatment of
chronic lymphocytic leukemia. Furthermore, the expression observed predominantly in
spleen cells also indicates that the polynucleotides or polypeptides are important in
treating and/or detecting hematopoietic disorders, such as graft versus host reaction,
graft versus host disease, transplant rejection, myelogenous leukemia, bone marrow
25 fibrosis, and myeloproliferative disease. The polypeptides or polynucleotides are also
useful to enhance or protect proliferation, differentiation, and functional activation of
hematopoietic progenitor cells (e.g., bone marrow cells), useful in treating cancer
patients undergoing chemotherapy or patients undergoing bone marrow transplantation.
The polypeptides or polynucleotides are also useful to increase the proliferation of
30 peripheral blood leukocytes, which can be used in the combat of a range of
hematopoietic disorders, including immunodeficiency diseases, leukemia, and
septicemia.

 Many polynucleotide sequences, such as EST sequences, are publicly available
and accessible through sequence databases. Some of these sequences are related to SEQ
35 ID NO:132 and may have been publicly available prior to conception of the present
invention. Preferably, such related polynucleotides are specifically excluded from the
scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 715 of SEQ ID NO:132, b is an integer of 15 to 729, where both a and b correspond to the positions of nucleotide residues shown in
5 SEQ ID NO:132, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 123

10 This gene is expressed primarily in neutrophils, dendritic cells, and CD34 positive cells (Cord Blood).

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
15 not limited to, immune, hematopoietic, or developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain
20 tissues or cell types (e.g. immune, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of some types of immune disorders, especially those involving neutrophils. More generally, as evidenced by expression in CD34 positive cells, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the numbers of stem cells and committed
30 progenitors. Expression of this gene product in primary dendritic cells also indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available
35 and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:133 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1065 of SEQ ID NO:133, b is an integer of 15
5 to 1079, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:133, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 124

10

This gene is expressed primarily in adult lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
15 not limited to, respiratory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the respiratory system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.
20 respiratory, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 The tissue distribution in lung tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of respiratory disorders, such as asthma, emphysema, and ARDS. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

30 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:134 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

35 Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1283 of SEQ ID NO:134. b is an integer of 15

to 1297, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:134, and where b is greater than or equal to a + 14.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 125

The gene encoding the disclosed cDNA is thought to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

10 This gene is expressed primarily in T-cell lymphoma and fetal liver/spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, developmental, or hematopoietic disorders, particularly
15 lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, developmental, and cancerous
20 and wounded tissues) or bodily fluids (e.g. lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:284 as residues: Gln-25 to Phe-43.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of T-cell lymphoma. Furthermore, expression of this gene product in fetal liver/spleen indicates a role in the
30 regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin,
35 the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma,

immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:135 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 603 of SEQ ID NO:135, b is an integer of 15 to 617, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:135, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 126

The translation product of this gene shares sequence homology with C9, a gene of unknown function. The gene encoding the disclosed cDNA is thought to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3. One embodiment of this gene comprises the polypeptides of the following amino acid sequence:

GTAFQHAFSTNDCSRNVYIKKNGFTLHRNPFAQSTDGARTKIGFSEGRHAWEV
WWEGLPLGTVAVIGIATKRAPMQCQGYVALLGSDDQSWGWNLVNLLHNGE
VNGSFPQCNNAPKYQIGERIRVILDMEDKTLAFERGYEFLGVAFRGLPKVCLYP
AVSAVYGNTTEVTLVYLGKPLDG (SEQ ID NO:477). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in placenta, and to a lesser extent, in apoptotic T-cells, as well as in smooth muscle, testes, and microvascular endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, reproductive, muscular, vascular, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, amniotic fluid, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells combined with the homology to the C9 protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some immune disorders, especially those involving T-cells. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses), or male infertility. Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO: 136 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1297 of SEQ ID NO: 136, b is an integer of 15 to 1311, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 136, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 127

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some immune disorders, especially those involving neutrophils. Furthermore, as evidenced by expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:137 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1081 of SEQ ID NO:137, b is an integer of 15 to 1095, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:137, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 128

This gene is expressed primarily in neutrophils; IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:287 as residues: Lys-36 to Asp-42.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some immune disorders, especially those involving neutrophils. Furthermore, as evidenced by the expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:138 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 678 of SEQ ID NO:138, b is an integer of 15 to 692, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:138, and where b is greater than or equal to a + 14.

35

FEATURES OF PROTEIN ENCODED BY GENE NO: 129

This gene is expressed primarily in neutrophils, IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:288 as residues: Pro-32 to Gln-38, Gly-51 to Asp-57.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of certain immune disorders, especially those involving neutrophils. Furthermore, as evidenced by expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:139 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 734 of SEQ ID NO:139, b is an integer of 15

to 748, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:139, and where b is greater than or equal to a + 14.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 130

This gene is expressed primarily in neutrophils, IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:289 as residues: Gly-22 to Ser-28.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of certain immune disorders involving neutrophils. Furthermore, as evidenced by expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:140 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1118 of SEQ ID NO:140, b is an integer of 15 to 1132, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:140, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 131

10 This gene is expressed primarily in corpus callosum.

 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly diseases of the brain, such as
15 neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. brain, and
20 cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 The tissue distribution in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of brain disorders and diseases, including paranoia, schizophrenia, depression, mania, and Alzheimer's disease. Furthermore, elevated expression of this gene product within the corpus callosum of the brain indicates that it may be involved in neuronal survival;
30 synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. Again, it may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

35 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:141 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of
5 a-b, where a is any integer between 1 to 1098 of SEQ ID NO:141, b is an integer of 15 to 1112, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:141, and where b is greater than or equal to a + 14.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 132

The translation product of this gene shares sequence homology with the putative transposase of the Tigger-1 transposon.

This gene is expressed primarily in atrophic endometrium.

15 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, muscular disorders, particularly muscular atrophy. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing
20 immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, muscular, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid
25 and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in endometrial tissue combine with the homology to a transposase indicates that polynucleotides and polypeptides corresponding to this gene
30 are useful for DNA repair in atrophying tissue, particularly of the endometrium. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ
35 ID NO:142 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1070 of SEQ ID NO:142, b is an integer of 15 to 1084, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:142, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 133

10 In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ARAFQHLMVADHSHFHRTLIKQPSMIPNATFYHIF (SEQ ID NO:478). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in hemangiopericytoma.

15 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, soft tissue tumors, particularly hemangiopericytoma, or other proliferative disorders. Similarly, polypeptides and antibodies directed to these
20 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid
25 and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:292 as residues: Ser-39 to Ser-44.

30 The tissue distribution in hemangiopericytoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of various soft-tissue tumors, in addition to other proliferative disorders which may afflict other tissues or cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed
35 tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:143 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more

- 5 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1036 of SEQ ID NO:143, b is an integer of 15 to 1050, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:143, and where b is greater than or equal to a + 14.

10

FEATURES OF PROTEIN ENCODED BY GENE NO: 134

This gene is expressed primarily in hypothalamus of a schizophrenic patient, and to a lesser extent in spleen.

- 15 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or immune disorders, particularly Schizophrenia or neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these
- 20 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, immune, hematopoietic, spleen, cancerous and wounded tissues) or bodily
- 25 fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- The tissue distribution in hypothalamus indicates that polynucleotides and
- 30 polypeptides corresponding to this gene are useful for diagnosis and treatment of Schizophrenia, as well as other central nervous system and immune system disorders. Furthermore, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease,
- 35 Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania,

dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, disorders of the endocrine system, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:144 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1099 of SEQ ID NO:144, b is an integer of 15 to 1113, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:144, and where b is greater than or equal to a + 14.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 135

The translation product of this gene shares sequence homology with a chicken ring-finger-zinc finger protein, C-RZF, in addition to, the human multiple membrane spanning receptor TRC8 which is thought to serve as a signaling receptor in renal and thyroid carcinomas. (See Genbank Accession No.gil3395787 (AF064801)) The TRC8 locus has been described in a family with classical features of hereditary renal cell carcinoma. The 8q24.1 (locus of TRC8) breakpoint region encodes the 664-aa multiple membrane spanning protein, TRC8, with similarity to the hereditary basal cell carcinoma/segment polarity gene, patched. This similarity involves two regions of patched, the putative sterol-sensing domain and the second extracellular loop that participates in the binding of sonic hedgehog. In the 3:8 translocation, TRC8 is fused to FHIT (fragile histidine triad gene) and is disrupted within the sterol-sensing domain. In

contrast, the FHIT coding region is maintained and expressed. In a series of sporadic renal carcinomas, an acquired TRC8 mutation was identified. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

ARALPEIKGSRLQEINDVCAICYHEFTTSARITPCNHYFHALCLRKWLVIQDTC
5 MCHQKVYIEDDIKDN

SNVSNNNGFIPPNETPEEAVREAAAESDRELNEDDSTDCDDDVQRRERNGVIQHT
GAAAGRI (SEQ ID NO:479), FSTQAQQLEEFNDDTD (SEQ ID NO:480), RLQE
INDVCAICYHEFTTSARI (SEQ ID NO:481), LYIQDTCPMCHQKVYIEDDI (SEQ
ID NO:482), VSNNNGFIPPNETPEEAVREA (SEQ ID NO:483), and/or DDSTDCD
10 DDVQRRERNGVIQHTGAAAG (SEQ ID NO:484). Polynucleotides encoding these
polypeptides are also encompassed by the invention. The gene encoding the disclosed
cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to
this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in human embryonic tissues.

15 Therefore, polynucleotides and polypeptides of the invention are useful as
reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, developmental abnormalities, particularly congenital defects or
proliferative conditions. Similarly, polypeptides and antibodies directed to these
20 polypeptides are useful in providing immunological probes for differential identification
of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,
particularly of the embryonic tissues, expression of this gene at significantly higher or
lower levels may be detected in certain tissues or cell types (e.g. developmental, renal,
endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic
25 fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell
sample taken from an individual having such a disorder, relative to the standard gene
expression level, i.e., the expression level in healthy tissue or bodily fluid from an
individual not having the disorder.

The tissue distribution in embryonic tissue, combined with the homology to ring
30 finger-zinc finger protein and the human TRC8 receptor indicates that polynucleotides
and polypeptides corresponding to this gene are useful for diagnosis and treatment of
abnormalities of the embryonic tissues, in particular proliferative disorders. In addition,
polynucleotides and polypeptides corresponding to this gene are useful for the
diagnosis, detection, and/or treatment of developmental disorders. The relatively
35 specific expression of this gene product during embryogenesis indicates that it may be a
key player in the proliferation, maintenance, and/or differentiation of various cell types
during development. It may also act as a morphogen to control cell and tissue type

specification. Because of potential roles in proliferation and differentiation, this gene product may have applications in the adult for tissue regeneration and the treatment of cancers. Moreover, this protein may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:145 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 671 of SEQ ID NO:145, b is an integer of 15 to 685, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:145, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 136

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: VAGITGAHHHAQLIFVLLVEMGFHHV GQAGLKLLTSDN PRTSASQSAGITGMSXGRRITCGQEFKTA VSYNCTTALQPDRAKLCFLFKKKK KISIQ RTLPGIKRVIYNYERVDSSKGHNSQVQWAHA CNPSTLGGRGGQIV (SEQ ID NO:485), AGITGAHHHAQLIFVLLVEMGF (SEQ ID NO:486), RVIYNYERVDSSKGHNSQVQWAHACNP (SEQ ID NO:487). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in microvascular endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, vascular or endothelial disorders, such as the following: arteriosclerosis, tumorigenesis, stroke, embolism, aneurysm, microvascular disease, and various cardiovascular disorders. Similarly, polypeptides and antibodies directed to these

polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. vascular, endothelial, cardiovascular, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in microvascular endothelial tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of vascular disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:146 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1024 of SEQ ID NO:146, b is an integer of 15 to 1038, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:146, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 137

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in fetal tissues, most notably fetal cochlea and fetal lung, and to a lesser extent, in rhabdomyosarcoma and healing groin wound tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, embryological/developmental abnormalities; hearing defects; respiratory diseases; rhabdomyosarcoma; general cancers and other proliferative conditions; fibrosis; wound healing. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryo/fetus or of striated muscle cells, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developmental, pulmonary, auditory, muscle, fibroid, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder

The tissue distribution in fetal tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diseases involving abnormal cellular proliferation, such as cancer. Expression of this gene product in rapidly proliferating cells, such as those found in the embryo; in rhabdomyosarcomas; and in wound healing tissue, indicates that this gene may play a role in controlling or promoting cell proliferation. Alternately, expression of this gene in fetal tissues indicates that it may play a role in cellular development and differentiation, particularly of the auditory system as well as the lungs. Thus, this gene product may be useful in the treatment and/or diagnosis of hearing defects, as well as respiratory disorders. Expression of this gene product in rhabdomyosarcoma indicates that it may play a role in the progression of such cancers, and may also be involved in metastasis and/or angiogenesis. Additionally, expression in wound healing tissues again indicates a role in the proliferation of connective tissue types involved in wound healing, as well as in the fibrosis and scarring that accompanies the wound healing process. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:147 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 837 of SEQ ID NO:147, b is an integer of 15

to 851, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:147, and where b is greater than or equal to a + 14.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 138

The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

10 This gene is expressed primarily in adult brain, and to a lesser extent, in cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
15 not limited to, disorders and diseases of the brain, particularly neurodegenerative and behavior conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher
20 or lower levels may be detected in certain tissues or cell types (e.g. neural, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

25 Preferred epitopes include those comprising a sequence shown in SEQ ID NO:297 as residues: Pro-25 to Ser-30, Thr-36 to Ser-47.

The tissue distribution in neural tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders and diseases of the brain, particularly paranoia, Alzheimer's, depression,
30 schizophrenia, and mania. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal
35 cord injuries, ischemia and infarction, aneurysms, hemorrhages, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance,

and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO: 148 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 600 of SEQ ID NO: 148, b is an integer of 15 to 614, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 148, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 139

This gene is expressed primarily in cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly neurodegenerative disorders, such as Alzheimers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in cerebellum indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of brain diseases and disorders. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:149 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1186 of SEQ ID NO:149, b is an integer of 15 to 1200, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:149, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 140

This gene is expressed primarily in brain tissue of a patient with Alzheimer's disease, and to a lesser extent, in human adipose tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or adipose-related disorders, particularly neurodegenerative disorders, such as Alzheimer's disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential
5 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, metabolic, adipose, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or
10 cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neural and adipose tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis
15 and treatment of Alzheimer's disease and other nervous system disorders. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases,
20 peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this
25 gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo,
30 sexually-linked disorders, or disorders of the cardiovascular system. More specifically, the protein product of this gene may show utility in the treatment, diagnosis, and/or prevention of neural disorders which occur secondary to aberrations in fatty-acid metabolism, such as improper development of the myelin sheath of nerve cells, for example. Protein, as well as, antibodies directed against the protein may show utility as
35 a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:150 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more

- 5 polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 669 of SEQ ID NO:150, b is an integer of 15 to 683, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:150, and where b is greater than or equal to a + 14.

10

FEATURES OF PROTEIN ENCODED BY GENE NO: 141

This gene is expressed primarily in T cells.

- Therefore, polynucleotides and polypeptides of the invention are useful as
- 15 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly T cell leukemia, immunodeficiencies, and inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes
- 20 for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or
- 25 cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:300 as residues: Asn-62 to Leu-68.

- 30 The tissue distribution T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of T cell leukemia and other disorders of the immune system. Moreover, this gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the
- 35 regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene

product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosus, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:151 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 813 of SEQ ID NO:151, b is an integer of 15 to 827, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:151, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 142

The gene encoding the disclosed cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in the frontal lobe of the brain, and to a lesser extent, in synovial fluid and embryos.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental or neural disorders, particularly neurodegenerative, behavioral, and congenital abnormalities of the brain. Similarly, polypeptides and

antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:301 as residues: Gln-24 to Lys-31.

The tissue distribution in brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of abnormalities of the brain. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the skeletal or cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:152 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 821 of SEQ ID NO:152, b is an integer of 15 to 835, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:152, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 143

The gene encoding the disclosed cDNA is believed to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in osteoblasts.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal disorders, such as osteoporosis, and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.skeletal, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in osteoblasts indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment of osteoporosis and other bone degenerative diseases. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:153 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 544 of SEQ ID NO:153, b is an integer of 15 to 558, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:153, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 144

This gene is expressed primarily in CD34 positive cells (cord blood) and placenta.

10 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and immune disorders, particularly proliferative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are
15 useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, reproductive, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid,
20 serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in cord blood and placental tissues indicates that
25 polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of certain immune disorders, especially those involving CD34 cells. Expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly,
30 developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

35 Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:154 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1187 of SEQ ID NO:154, b is an integer of 15 to 1201, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:154, and where b is greater than or equal to a + 14.

10 FEATURES OF PROTEIN ENCODED BY GENE NO: 145

This gene is expressed primarily in frontal cortex of the brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or spinal cord disorders, such as neurodegenerative conditions and other abnormalities of the brain. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:304 as residues: Pro-21 to Ser-27.

The tissue distribution in frontal cortex tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of the abnormalities of the brain. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive

disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:155 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1012 of SEQ ID NO:155, b is an integer of 15 to 1026, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:155, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 146

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in adrenal gland tumor, breast tissue, and to a lesser extent in adipose tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine or reproductive disorders, such as adrenal gland tumor; breast cancer; metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the adrenal glands and breast, expression of this gene at significantly

higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, metabolic, endocrine, breast, adrenal gland, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, breast milk, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:305 as residues: Arg-44 to Lys-49, Asp-60 to Phe-66.

The tissue distribution in adrenal gland and breast tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders involving the adrenal gland. Expression of this gene product in adrenal gland tumor indicates that it may play a role in the proliferation of cells of the adrenal gland, or potentially in the proliferation of cells in general. In such an event, it may play a role in determining the course and severity of cancer. Alternatively, it may play a role in the normal function of adrenal glands, such as in the production of corticosteroids, androgens, or epinephrines. Thus it may play a role in general homeostasis, as well as in disorders involving the androgen hormones. Expression of this gene product in breast and adipose tissues also indicates that it may play a role in breast cancer, or in supplying vital nutrients to the infant during lactation. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:156 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 890 of SEQ ID NO:156, b is an integer of 15 to 904, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:156, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 147

This gene is expressed primarily in LNCAP, and untreated spleen; metastatic melanoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, integumentary disorders, such as metastatic melanoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and cancer metabolic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:306 as residues: His-47 to Thr-53.

The tissue distribution in spleen and integumentary tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some types of cancer, especially metastatic melanoma. The protein product of this gene is useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, urticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, athlete's foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chondromalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type

II, metaphyseal chondrodysplasia type Schmid). Alternatively, this gene is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:157 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 902 of SEQ ID NO:157, b is an integer of 15 to 916, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 148

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: AGAEVVMLFLLTPSS HHQHECVRRAFECGDCHILLDNNV LGVDCHGAGERAVHLEDHFVHIDTISLLLEDALEYSALIAGHPKSD LPPGLSRC RPWEHHWPISYTG (SEQ ID NO:488), TI SYLCNNVSYMQLQKLVGKSMIFLP YSLPIHLPGNHRLLLPRVGMRLRGCCFSPYIITDFKWC (SEQ ID NO:489), EMGQWCSQGLHLDSPGGKSDFGCPAINAEYSRASSKSRLMVSMWTKWSSRC TALSPAP (SEQ ID NO:490), RAFECGDCHILLDNNVLGVDCHGAG (SEQ ID NO:491), and/or LVGKSMIFLPYSLPIHLPGNHRL (SEQ ID NO:492).

Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1.

Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in ovary, and to a lesser extent in meninges, the adrenal gland, and the cerebellum.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, neural, and endocrine disorders, such as ovarian and brain cancers, neurodeficiency disorders, and infertility. Similarly, polypeptides and
10 antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive and endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. neural, reproductive, ovarian, and cancerous and
15 wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

20 The tissue distribution in ovarian and endocrine tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer and other endocrine disorders. Alternatively, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or
25 inflammatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning
30 disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or
35 survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well

as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

- Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:158 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 907 of SEQ ID NO:158, b is an integer of 15 to 921, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14.

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
1	HNGEU17	209299 09/25/97	Uni-ZAP XR	11	826	1	826	277	277	160	1	17	18	23
2	HNGDJ72	209299 09/25/97	Uni-ZAP XR	12	524	1	524	185	185	161	1	19	20	113
3	HNGEO29	209299 09/25/97	Uni-ZAP XR	13	491	1	491	98	98	162	1	32	33	44
4	HNHDL95	209299 09/25/97	Uni-ZAP XR	14	403	1	403	121	121	163	1	23	24	58
5	HAGDS35	209299 09/25/97	Uni-ZAP XR	15	813	1	813	52	52	164	1	23	24	118
6	HNGEQ48	209299 09/25/97	Uni-ZAP XR	16	264	1	264	10	10	165	1	20	21	54
7	HNGDG40	209299 09/25/97	Uni-ZAP XR	17	520	1	520	13	13	166	1	36	37	127

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
8	HNGEN81	209299 09/25/97	Uni-ZAP XR	18	993	1	993	380	380	167	1	25	26	56
9	H2MAC30	209299 09/25/97	pBluescript SK-	19	459	1	459	157	157	168	1	28	29	72
10	hnhfb16	209299 09/25/97	Uni-ZAP XR	20	555	1	555	344	344	169	1	23	24	70
11	HPFCL43	209299 09/25/97	Uni-ZAP XR	21	665	1	665	21	21	170	1	17	18	79
12	HSATR82	209299 09/25/97	Uni-ZAP XR	22	777	1	777	74	74	171	1	15	16	41
13	H6EDF66	209299 09/25/97	Uni-ZAP XR	23	540	1	540	146	146	172	1	27	28	131
14	HNHIC21	209299 09/25/97	Uni-ZAP XR	24	484	1	484	65	65	173	1	16	17	44
15	HOVCA92	209299 09/25/97	pSport1	25	707	1	488	181	181	174	1	20	21	62

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
16	HNHDW38	209299 09/25/97	Uni-ZAP XR	26	793	1	793	66	66	175	1	19	20	19
17	HSDIL30	209299 09/25/97	Uni-ZAP XR	27	638	1	638	26	26	176	1	33	34	40
18	HATDB65	209299 09/25/97	Uni-ZAP XR	28	528	14	528	110	110	177	1	40	41	48
19	HPMSM14	209299 09/25/97	pBluescript	29	919	1	919	119	119	178	1	46	47	106
20	HTTEA24	209299 09/25/97	Uni-ZAP XR	30	864	1	864	133	133	179	1	20	21	45
21	HAGDS20	209299 09/25/97	Uni-ZAP XR	31	919	1	919	11	11	180	1	17	18	66
22	HSDJM30	209299 09/25/97	Uni-ZAP XR	32	956	1	956	70	70	181	1	24	25	49
23	HNHEE88	209299 09/25/97	Uni-ZAP XR	33	566	1	566	87	87	182	1	19	20	72

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
24	HSLFD55	209346 10/09/97	Uni-ZAP XR	34	1564	1	1564	105	183	1	21	22	43
25	HSAXJ29	209299 09/25/97	Uni-ZAP XR	35	1035	1	1035	129	184	1	19	20	57
26	HSFAM39	209299 09/25/97	Uni-ZAP XR	36	620	1	620	117	185	1	23	24	68
27	HTODO72	209299 09/25/97	Uni-ZAP XR	37	973	1	973	183	186	1	16	17	24
28	HADDZ85	209299 09/25/97	pSport1	38	838	1	838	270	187	1	36	37	57
29	HDPCM26	209300 09/25/97	pCMVSPORT 3.0	39	607	1	607	174	188	1	19	20	66
30	HSZAA13	209300 09/25/97	Uni-ZAP XR	40	882	1	855	147	189	1	19	20	88
31	HDTBP04	209300 09/25/97	pCMVSPORT 2.0	41	959	1	959	65	190	1	15	16	220

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
32	HHGCQ54	209300 09/25/97	Lambda ZAP II	42	875	1	875	62	62	191	1	15	16	51
33	HSNAB12	209300 09/25/97	Uni-ZAP XR	43	630	1	630	151	151	192	1	27	28	71
34	HBJID05	209300 09/25/97	Uni-ZAP XR	44	571	1	571	137	137	193	1	20	21	111
35	HSNBM49	209300 09/25/97	Uni-ZAP XR	45	930	1	930	27	27	194	1	21	22	60
36	HJMBF77	209300 09/25/97	pCMV Sport 3.0	46	437	1	432	60	60	195	1	24	25	126
37	HJMBM38	209300 09/25/97	pCMV Sport 3.0	47	1024	316	1023	387	387	196	1	15	16	112
38	HHGCL33	209300 09/25/97	Lambda ZAP II	48	463	1	463	74	74	197	1	20	21	65
39	HCEWE20	209300 09/25/97	Uni-ZAP XR	49	885	13	885	166	166	198	1	18	19	51

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of 5' NT Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
40	HCUHL13	209300 09/25/97	ZAP Express	50	847	1	847	84	84	199	1	20	21	58
41	HBJHO68	209300 09/25/97	Uni-ZAP XR	51	580	1	580	34	34	200	1	24	25	51
42	HCWDV84	209300 09/25/97	ZAP Express	52	598	1	598	47	47	201	1	25	26	80
43	HBXFC78	209300 09/25/97	ZAP Express	53	571	1	567	184	184	202	1	14	15	69
44	HE2FI45	209300 09/25/97	Uni-ZAP XR	54	1247	212	1082	273	273	203	1	38	39	45
45	HEOMG13	209300 09/25/97	pSport1	55	848	182	848	247	247	204	1	27	28	52
46	HFAMH77	209300 09/25/97	Uni-ZAP XR	56	669	96	669	240	240	205	1	33	34	61
47	HSVCF20	209300 09/25/97	Uni-ZAP XR	57	680	1	680	43	43	206	1	25	26	43

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	5' NT 3' NT of Clone Seq.	5' NT of Start Codon	5' NT of AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
48	HISAG02	209300 09/25/97	pSport1	58	524	1	524	18	18	207	1	27	28	40
49	HCDAF84	209300 09/25/97	Uni-ZAP XR	59	427	1	427	168	168	208	1	18	19	56
50	HHAAC17	209300 09/25/97	Uni-ZAP XR	60	1263	1	1263	227	227	209	1	19	20	125
51	HSNMC45	209300 09/25/97	Uni-ZAP XR	61	720	1	720	232	232	210	1	19	20	25
52	HEQAG39	209300 09/25/97	pCMV Sport 3.0	62	589	69	589	93	93	211	1	19	20	47
53	HKACH44	209300 09/25/97	pCMV Sport 2.0	63	686	1	686	375	375	212	1	25	26	44
54	HBNBG49	209300 09/25/97	Uni-ZAP XR	64	452	1	452	40	40	213	1	34	35	51
55	HE2EN04	209300 09/25/97	Uni-ZAP XR	65	370	1	370	57	57	214	1	16	17	50

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of 5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
56	HSVAA10	209300 09/25/97	Uni-ZAP XR	66	987	1	987	38	38	215	1	16	17	209
57	HFPBA88	209300 09/25/97	Uni-ZAP XR	67	1018	284	1018	33	33	216	1	38	39	195
57	HFPBA88	209300 09/25/97	Uni-ZAP XR	159	804	70	804	98	98	308	1	41	42	102
58	HFTBM50	209300 09/25/97	Uni-ZAP XR	68	762	1	740	158	158	217	1	20	21	34
59	HHEBW54	209300 09/25/97	pCMVSPORT 3.0	69	630	1	630	97	97	218	1	37	38	71
60	HFEHB21	209300 09/25/97	Uni-ZAP XR	70	940	1	940	21	21	219	1	30	31	52
61	HFTDZ36	209300 09/25/97	Uni-ZAP XR	71	1103	231	1103	547	547	220	1	22	23	68
62	HGLAW96	209300 09/25/97	Uni-ZAP XR	72	899	246	899	308	308	221	1	24	25	68

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	5' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
63	HKAFK41	209300 09/25/97	pCMVSPORT 2.0	73	549	1	549	243	243	222	1	30	31	43
64	HOSEG51	209324 10/02/97	Uni-ZAP XR	74	590	48	590	232	232	223	1	31	32	102
65	HTEJT39	209324 10/02/97	Uni-ZAP XR	75	1056	1	1056	146	146	224	1	32	33	213
66	HPTRH45	209324 10/02/97	pBluescript	76	930	1	930	92	92	225	1	26	27	108
67	HDHMA72	209324 10/02/97	pCMVSPORT 2.0	77	4463	216	2158	287	287	226	1	36	37	315
68	HNTBL27	209324 10/02/97	pCMVSPORT 3.0	78	791	71	791	100	100	227	1	23	24	115
69	HCFMX35	209324 10/02/97	pSPORT	79	1292	1	1292	160	160	228	1	21	22	106
70	HMSFS21	209324 10/02/97	Uni-ZAP XR	80	1283	1	1283	28	28	229	1	17	18	37

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of 5' NT Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
71	HMUAO21	209324 10/02/97	pCMVSPORT 3.0	81	708	245	708	289	289	230	1	25	26	67
72	HCHAR28	209324 10/02/97	pSport1	82	1464	325	1463	482	482	231	1	46	47	50
73	HLYDU25	209324 10/02/97	pSport1	83	616	1	616	250	250	232	1	22	23	40
74	HOEJH89	209324 10/02/97	Uni-ZAP XR	84	928	18	903	25	25	233	1	19	20	41
75	HPFDG48	209324 10/02/97	Uni-ZAP XR	85	723	165	700	283	283	234	1	18	19	47
76	HWBIM18	209324 10/02/97	Uni-ZAP XR	86	570	1	570	45	45	235	1	21	22	39
77	HCFOM18	209324 10/02/97	pSport1	87	639	1	639	28	28	236	1	20	21	63
78	HMWFO02	209324 10/02/97	Uni-Zap XR	88	708	1	708	20	20	237	1	38	39	60

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
79	HNGAV42	209324 10/02/97	Uni-ZAP XR	89	949	1	949	278	278	238	1	28	29	62
80	HL3AB91	209324 10/02/97	Uni-ZAP XR	90	1171	1	1171	158	158	239	1	21	22	56
81	HSDSE75	209324 10/02/97	pBluescript	91	1151	1	1151	160	160	240	1	18	19	181
82	HLMFD85	209324 10/02/97	Lambda ZAP II	92	714	1	714	33	33	241	1	27	28	70
83	HLQCI74	209324 10/02/97	Lambda ZAP II	93	810	1	810	261	261	242	1	17	18	61
84	HLQCK07	209324 10/02/97	Lambda ZAP II	94	1176	1	1176	410	410	243	1	18	19	34
85	HTEFU65	209324 10/02/97	Uni-ZAP XR	95	1028	1	1028	231	231	244	1	24	25	46
86	HLYBF22	209324 10/02/97	pSportI	96	747	1	747	39	39	245	1	32	33	50

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
87	HMDAP35	209324 10/02/97	Uni-ZAP XR	97	628	1	628	70	70	246	1	21	22	50
88	HTOJK60	209324 10/02/97	Uni-ZAP XR	98	904	1	904	217	217	247	1	19	20	32
89	HWBCN75	209324 10/02/97	pCMVSPORT 3.0	99	576	1	576	184	184	248	1	34	35	48
90	HROAH06	209324 10/02/97	Uni-ZAP XR	100	713	1	713	29	29	249	1	43	44	115
91	HSAXA83	209324 10/02/97	Uni-ZAP XR	101	649	1	649	92	92	250	1	22	23	74
92	HSDJE10	209324 10/02/97	Uni-ZAP XR	102	697	1	697	157	157	251	1	21	22	62
93	HBAMA40	209324 10/02/97	pSport1	103	1288	1	1288	95	95	252	1	31	32	72
94	HBAMB34	209324 10/02/97	pSport1	104	1027	1	1027	87	87	253	1	35	36	48

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
95	HCWK15	209324 10/02/97	ZAP Express	105	710	1	710	37	37	254	1	18	19	40
96	HDTDM65	209324 10/02/97	pCMV Sport 2.0	106	530	1	530	159	159	255	1	40	41	53
97	HMMBF71	209324 10/02/97	pSport1	107	392	1	392	153	153	256	1	24	25	40
98	HPBDH41	209324 10/02/97	pBluescript SK-	108	991	288	991	373	373	257	1	15	16	41
99	HPBEN24	209324 10/02/97	pBluescript SK-	109	912	363	912	541	541	258	1	20	21	52
100	HCUIM65	209324 10/02/97	ZAP Express	110	875	331	736	557	557	259	1	27	28	47
101	HKNA95	209324 10/02/97	pBluescript SK-	111	459	1	459	114	114	260	1	28	29	52
102	HKIYH57	209324 10/02/97	pBluescript	112	609	156	609	336	336	261	1	23	24	54

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
103	HBIBW67	209324 10/02/97	Uni-ZAP XR	113	1404	1	1404	685	685	262	1	33	34	38
104	HCFCU88	209324 10/02/97	pSport1	114	853	1	853	326	326	263	1	14	15	23
105	HBJMG49	209324 10/02/97	Uni-ZAP XR	115	845	1	804	53	53	264	1	17	18	46
106	H6EDC19	209324 10/02/97	Uni-ZAP XR	116	760	324	760	389	389	265	1	25	26	114
107	HSKHZ81	209346 10/09/97	pBluescript	117	988	1	967	57	57	266	1	27	28	247
108	HBJFX78	209346 10/09/97	Uni-ZAP XR	118	1947	1	1947	34	34	267	1	18	19	177
109	HEMFS60	209346 10/09/97	Uni-ZAP XR	119	1448	63	1448	111	111	268	1	17	18	78
110	HKACB56	209346 10/09/97	pCMVSPORT 2.0	120	496	1	496	27	27	269	1	23	24	80

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
111	HTXJX80	209346 10/09/97	Uni-ZAP XR	121	1174	16	880	206	206	270	1	26	27	68
112	HAFBD61	209346 10/09/97	pBluescript SK-	122	1046	1	1046	210	210	271	1	22	23	130
113	HBJU28	209346 10/09/97	Uni-ZAP XR	123	1160	1	1160	133	133	272	1	18	19	84
114	HINHE147	209346 10/09/97	Uni-ZAP XR	124	893	1	893	192	192	273	1	18	19	78
115	HPMFY74	209346 10/09/97	Uni-ZAP XR	125	1049	1	1049	91	91	274	1	40	41	53
116	HKACD58	209346 10/09/97	pCMVSPORT 2.0	126	1626	1	1626	35	35	275	1	25	26	154
117	HLDBB60	209346 10/09/97	pCMVSPORT 3.0	127	1177	1	1177	283	283	276	1	20	21	128
118	HLYP91	209346 10/09/97	pSPORT1	128	1276	1	1276	280	280	277	1	29	30	83

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
119	HSKNB56	209346 10/09/97	pBluescript	129	1334	449	1334	484	278	1	25	26	85
120	HHGCW91	209346 10/09/97	Lambda ZAP II	130	532	1	532	107	279	1	18	19	95
121	HKIYE96	209346 10/09/97	pBluescript	131	685	145	685	284	280	1	19	20	97
122	HLYAN59	209346 10/09/97	pSport1	132	729	1	729	254	281	1	40	41	54
123	HNEEE24	209346 10/09/97	Uni-ZAP XR	133	1079	1	1079	213	282	1	21	22	71
124	HAPRK85	209346 10/09/97	Uni-ZAP XR	134	1297	1	1297	175	283	1	29	30	43
125	HLTEJ06	209346 10/09/97	Uni-ZAP XR	135	617	69	617	197	284	1	22	23	55
126	HMEKT48	209346 10/09/97	Lambda ZAP II	136	1311	1	1115	47	285	1	19	20	48

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
127	HNGHR74	209346 10/09/97	Uni-ZAP XR	137	1095	1	1095	53	53	286	1	18	19	41
128	HNHED17	209346 10/09/97	Uni-ZAP XR	138	692	1	692	282	282	287	1	19	20	48
129	HNHEP59	209346 10/09/97	Uni-ZAP XR	139	748	1	748	247	247	288	1	27	28	109
130	HNHFJ25	209346 10/09/97	Uni-ZAP XR	140	1132	1	1132	145	145	289	1	22	23	63
131	HCPAA69	209346 10/09/97	Uni-ZAP XR	141	1112	1	1112	8	8	290	1	20	21	41
132	HEAAR07	209346 10/09/97	Uni-ZAP XR	142	1084	1	1084	48	48	291	1	31	32	42
133	HHGDW43	209346 10/09/97	Lambda ZAP II	143	1050	1	1050	107	107	292	1	41	42	44
134	HHSDX28	209346 10/09/97	Uni-ZAP XR	144	1113	1	1113	90	90	293	1	21	22	56

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
135	HE8ER60	209346 10/09/97	Uni-ZAP XR	145	685	1	685	48	48	294	1	32	33	74
136	HMEJQ66	209346 10/09/97	Lambda ZAP II	146	1038	1	1038	80	80	295	1	24	25	50
137	HRDAD66	209346 10/09/97	Uni-ZAP XR	147	851	99	851	269	269	296	1	33	34	44
138	HCMST14	209346 10/09/97	Uni-ZAP XR	148	614	1	614	136	136	297	1	24	25	47
139	HCEBA03	209346 10/09/97	Uni-ZAP XR	149	1200	1	1200	76	76	298	1	21	22	54
140	HFAAH18	209346 10/09/97	Uni-ZAP XR	150	683	79	683	304	304	299	1	21	22	29
141	HJAAM10	209346 10/09/97	pBluescript SK-	151	827	135	827	320	320	300	1	35	36	72
142	HFIBV09	209346 10/09/97	pSport1	152	835	129	835	370	370	301	1	17	18	36

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
143	HOHCC74	209346 10/09/97	pCMVSPORT 2.0	153	558	1	558	327	327	302	1	20	21	48
144	HPMFY57	209346 10/09/97	Uni-ZAP XR	154	1201	1	1201	250	250	303	1	30	31	42
145	HFXDN63	209346 10/09/97	Lambda ZAP II	155	1026	1	1026	33	33	304	1	14	15	53
146	HADCL76	209346 10/09/97	pSPORT1	156	904	1	904	108	108	305	1	29	30	75
147	HMMAS76	209346 10/09/97	pSPORT1	157	916	1	916	13	13	306	1	29	30	62
148	HMKCG09	209346 10/09/97	pSPORT1	158	921	60	921	221	221	307	1	28	29	49

Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." and the "3' NT of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to the secreted proteins encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are species homologs. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below).

It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

- 5 The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified by the one-step method described in Smith and Johnson, *Gene* 67:31-40 (1988). Polypeptides of the invention also can be purified from natural or recombinant sources
- 10 using antibodies of the invention raised against the secreted protein in methods which are well known in the art.

Signal Sequences

- Methods for predicting whether a protein has a signal sequence, as well as the
- 15 cleavage point for that sequence, are available. For instance, the method of McGeoch, *Virus Res.* 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, *Nucleic Acids Res.* 14:4683-4690 (1986) uses the information
- 20 from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, *supra.*) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

- In the present case, the deduced amino acid sequence of the secreted polypeptide
- 25 was analyzed by a computer program called SignalP (Henrik Nielsen et al., *Protein Engineering* 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results
- 30 shown in Table 1.

- As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., +
- 35 or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely

uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

10 **Polynucleotide and Polypeptide Variants**

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

15 By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown in Table 1, the ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are:

35 Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization

Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05. Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query

amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions,

5 interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequences shown in Table 1 or to the amino acid sequence encoded by deposited DNA clone can be
10 determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and
15 subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window
20 Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity.
25 For subject sequences truncated at the N- and C-termini, relative to the the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of
30 the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are
35 considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired
5 residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence.
10 This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query
15 sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or
20 activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in
25 the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level.

30 Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be
35 deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., *J. Biol. Chem.* 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after

deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

Polynucleotide and Polypeptide Fragments

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-

60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred.

- 5 Similarly, polynucleotide fragments encoding these polypeptide fragments are also preferred.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotide fragments encoding these domains are also contemplated.

Other preferred fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Epitopes & Antibodies

In the present invention, "epitopes" refer to polypeptide fragments having antigenic or immunogenic activity in an animal, especially in a human. A preferred embodiment of the present invention relates to a polypeptide fragment comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response. (See, for instance, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983).)

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

In the present invention, antigenic epitopes preferably contain a sequence of at least seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe, J. G. et al., Science 219:660-666 (1983).)

Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow, M. et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle, F. J. et al., J. Gen. Virol. 66:2347-2354 (1985).) A preferred immunogenic epitope includes
5 the secreted protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a
10 denatured polypeptide (e.g., in Western blotting.)

As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')₂ fragments) which are capable of specifically binding to protein. Fab and F(ab')₂ fragments lack the Fc fragment of intact antibody, clear more rapidly from
15 the circulation, and may have less non-specific tissue binding than an intact antibody. (Wahl et al., J. Nucl. Med. 24:316-325 (1983).) Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies.

20

Fusion Proteins

Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the
25 polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention
30 include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino
35 acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the

polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., *Nature* 331:84-86 (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG) can also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., *J. Biochem.* 270:3958-3964 (1995).)

Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., *J. Molecular Recognition* 8:52-58 (1995); K. Johanson et al., *J. Biol. Chem.* 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., *Proc. Natl. Acad. Sci. USA* 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., *Cell* 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells; insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods
5 In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography,
10 phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also
15 be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production
20 procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein
25 after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

30 Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The polynucleotides of the present invention are useful for chromosome
35 identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat

polymorphisms), are presently available. Each polynucleotide of the present invention can be used as a chromosome marker.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be
5 selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the
10 polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, and preselection by hybridization to construct chromosome
15 specific-cDNA libraries.

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al.,
20 "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes). Preferred polynucleotides
25 correspond to the noncoding regions of the cDNAs because the coding sequences are more likely conserved within gene families, thus increasing the chance of cross hybridization during chromosomal mapping.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage
30 analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) .) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease
35 could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined.

First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the
5 mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected
10 individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

In addition to the foregoing, a polynucleotide can be used to control gene
15 expression through triple helix formation or antisense DNA or RNA. Both methods rely on binding of the polynucleotide to DNA or RNA. For these techniques, preferred polynucleotides are usually 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science
20 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model
25 systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the
30 present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of
35 restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying

personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

5 The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this
10 technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

 Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as
15 tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more
20 restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

 There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of
25 unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

30 In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using
35 DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

5 A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-3096 (1987).) Other antibody-based methods useful for detecting protein gene
10 expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (^{125}I , ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium (^{112}In), and technetium ($^{99\text{m}}\text{Tc}$), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

15 In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for
20 NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, ^{131}I ,
25 ^{112}In , $^{99\text{m}}\text{Tc}$), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human
30 subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of $^{99\text{m}}\text{Tc}$. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The
35 Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder.

Moreover, polypeptides of the present invention can be used to treat disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B), to inhibit the activity of a polypeptide (e.g., an oncogene), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

Biological Activities

The polynucleotides and polypeptides of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides could be used to treat the associated disease.

Immune Activity

A polypeptide or polynucleotide of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the

proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders
5 may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, a polynucleotide or polypeptide of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

A polynucleotide or polypeptide of the present invention may be useful in
10 treating or detecting deficiencies or disorders of hematopoietic cells. A polypeptide or polynucleotide of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to:
15 blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, a polypeptide or polynucleotide of the present invention could also
20 be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, a polynucleotide or polypeptide of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet
25 disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, a polynucleotide or polypeptide of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

A polynucleotide or polypeptide of the present invention may also be useful in
30 treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of a polypeptide or polynucleotide of the
35 present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected by the present invention include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by a polypeptide or polynucleotide of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

A polynucleotide or polypeptide of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, a polypeptide or polynucleotide of the present invention may also be used to modulate inflammation. For example, the polypeptide or polynucleotide may inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

Hyperproliferative Disorders

A polypeptide or polynucleotide can be used to treat or detect hyperproliferative disorders, including neoplasms. A polypeptide or polynucleotide of the present invention may inhibit the proliferation of the disorder through direct or indirect

interactions. Alternatively, a polypeptide or polynucleotide of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating,
5 or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

10 Examples of hyperproliferative disorders that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but are not limited to neoplasms located in the: abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system,
15 pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary
20 Syndrome, Waldenstrom's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

Infectious Disease

25 A polypeptide or polynucleotide of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, the
30 polypeptide or polynucleotide of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of viruses, include, but are not limited to the following
35 DNA and RNA viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes

Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza), Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following Gram-Negative and Gram-positive bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, Enterobacteriaceae (Klebsiella, Salmonella, Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Meningococcal), Pasteurellaceae Infections (e.g., Actinobacillus, Hemophilus, Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, and Staphylococcal. These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis, Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following families: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas. These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), Malaria, pregnancy complications, and toxoplasmosis. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Preferably, treatment using a polypeptide or polynucleotide of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

Regeneration

A polynucleotide or polypeptide of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vascular (including vascular endothelium), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, a polynucleotide or polypeptide of the present invention may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. A polynucleotide or polypeptide of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue

regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using a polynucleotide or polypeptide of the present invention to proliferate and differentiate
5 nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized
10 neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotide or polypeptide of the present invention.

15 **Chemotaxis**

A polynucleotide or polypeptide of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of
20 hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

A polynucleotide or polypeptide of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system
25 disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that a polynucleotide or polypeptide of the present
30 invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, a polynucleotide or polypeptide of the present invention could be used as an inhibitor of chemotaxis.

Binding Activity

35 A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit

(antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptide from suitably manipulated cells or tissues.

Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying
5 agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

Other Activities

10 A polypeptide or polynucleotide of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide or polynucleotide of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color,
15 skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide or polynucleotide of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide or polynucleotide of the present invention may be used to change
20 a mammal's mental state or physical state by influencing biorhythms, circadian rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

25 A polypeptide or polynucleotide of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

Other Preferred Embodiments

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1.

35 Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of

positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Clone Sequence and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous
5 nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Start Codon and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Similarly preferred is a nucleic acid molecule wherein said sequence of
10 contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide
15 sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide
sequence which is at least 95% identical to a sequence of at least about 500 contiguous
20 nucleotides in the nucleotide sequence of SEQ ID NO:X.

A further preferred embodiment is a nucleic acid molecule comprising a
nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ
ID NO:X beginning with the nucleotide at about the position of the 5' Nucleotide of the
First Amino Acid of the Signal Peptide and ending with the nucleotide at about the
25 position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in
Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising
a nucleotide sequence which is at least 95% identical to the complete nucleotide
sequence of SEQ ID NO:X.

Also preferred is an isolated nucleic acid molecule which hybridizes under
30 stringent hybridization conditions to a nucleic acid molecule, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which
35 comprises a human cDNA clone identified by a cDNA Clone Identifier in Table 1,
which DNA molecule is contained in the material deposited with the American Type

Culture Collection and given the ATCC Deposit Number shown in Table 1 for said cDNA Clone Identifier.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous
5 nucleotides in the nucleotide sequence of a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the deposit given the ATCC Deposit Number shown in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of the complete
10 open reading frame sequence encoded by said human cDNA clone.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising
15 a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by said human cDNA clone.

20 A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone
25 identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95%
30 identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of
35 comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1.

Also preferred is a polypeptide, wherein said sequence of contiguous amino acids is included in the amino acid sequence of SEQ ID NO:Y in the range of positions beginning with the residue at about the position of the First Amino Acid of the Secreted Portion and ending with the residue at about the Last Amino Acid of the Open Reading Frame as set forth for SEQ ID NO:Y in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a secreted portion of the secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide
5 comprises an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

10 Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

15 Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a secreted portion of a human secreted protein comprising an amino acid
20 sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y beginning with the residue at the position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y wherein Y is an integer set forth in Table 1 and said position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y is defined in Table 1; and an amino acid sequence of a secreted portion of a protein encoded by a human
25 cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a secreted protein activity, which method comprises administering to such an
30 individual a pharmaceutical composition comprising an amount of an isolated polypeptide, polynucleotide, or antibody of the claimed invention effective to increase the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of
35 illustration and are not intended as limiting.

Examples

Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

5 Each cDNA clone in a cited ATCC deposit is contained in a plasmid vector. Table 1 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The table immediately below correlates the related plasmid for each phage vector used in constructing the cDNA library. For
10 example, where a particular clone is identified in Table 1 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

	<u>Vector Used to Construct Library</u>	<u>Corresponding Deposited Plasmid</u>
	Lambda Zap	pBluescript (pBS)
	Uni-Zap XR	pBluescript (pBS)
15	Zap Express	pBK
	lafmid BA	plafmid BA
	pSport1	pSport1
	pCMVSPORT 2.0	pCMVSPORT 2.0
	pCMVSPORT 3.0	pCMVSPORT 3.0
20	pCR [®] 2.1	pCR [®] 2.1

 Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Altting-Mees, M. A. and Short, J. M., Nucleic Acids Res.
25 17:9494 (1989)) and pBK (Altting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS.
30 The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

35 Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain

DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., *Focus* 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 1, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited in Table 1 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone identified in Table 1. Typically, each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones.

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 1. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ³²P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the SEQ ID NO:X (i.e., within the region of SEQ ID NO:X bounded by the 5' NT and the 3' NT of the clone defined in Table 1) are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 μ l of reaction mixture with 0.5 μ g of the above cDNA template. A convenient reaction mixture is 1.5-5 mM MgCl_2 , 0.01% (w/v) gelatin, 20 μ M each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., *Nucleic Acids Res.* 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is

used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

5

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the cDNA sequence corresponding to SEQ ID NO:X., according to the method described in Example 1. (See also, Sambrook.)

10

Example 3: Tissue Distribution of Polypeptide

Tissue distribution of mRNA expression of polynucleotides of the present invention is determined using protocols for Northern blot analysis, described by, among others, Sambrook et al. For example, a cDNA probe produced by the method described in Example 1 is labeled with P³² using the rediprime™ DNA labeling system (Amersham Life Science), according to manufacturer's instructions. After labeling, the probe is purified using CHROMA SPIN-100™ column (Clontech Laboratories, Inc.), according to manufacturer's protocol number PT1200-1. The purified labeled probe is then used to examine various human tissues for mRNA expression.

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Multiple Tissue Northern (MTN) blots containing various human tissues (H) or human immune system tissues (IM) (Clontech) are examined with the labeled probe using ExpressHyb™ hybridization solution (Clontech) according to manufacturer's protocol number PT1190-1. Following hybridization and washing, the blots are mounted and exposed to film at -70°C overnight, and the films developed according to standard procedures.

25

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on

30

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either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

5 **Example 5: Bacterial Expression of a Polypeptide**

 A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as
10 BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site
15 (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

 The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses
20 the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

 Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml).
25 The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.⁶⁰⁰) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

30 Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from
35 QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high

affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed
5 with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The
10 recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer
15 plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a
20 neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (*lacIq*). The origin of replication (*oriC*) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR
25 primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.
30

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

35 **Example 6: Purification of a Polypeptide from an Inclusion Body**

The following alternative method can be used to purify a polypeptide expressed in *E. coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell
5 culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a
10 high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M
15 NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

20 Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

25 To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted
30 with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem

columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A_{280} monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 μ g of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

15 **Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System**

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak *Drosophila* promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., *Virology* 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon and the naturally associated leader sequence identified in Table 1, is amplified using the PCR protocol described in Example 1. If the naturally occurring

signal sequence is used to produce the secreted protein, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures,"

5 Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

10 The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

15 The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

20 Five μ g of a plasmid containing the polynucleotide is co-transfected with 1.0 μ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One μ g of BaculoGold™ virus DNA and 5 μ g of the plasmid are mixed in a sterile well of a
25 microtiter plate containing 50 μ l of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 μ l Lipofectin plus 90 μ l Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then
30 incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life
35 Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture

and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 µCi of ³⁵S-methionine and 5 µCi ³⁵S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

Example 8: Expression of a Polypeptide in Mammalian Cells

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLV, HIV and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSPORT 2.0, and pCMVSPORT 3.0. Mammalian host cells that could be used include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as dhfr, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

5 The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., *J. Biol. Chem.* 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., *Biochem. et Biophys. Acta*, 1097:107-143 (1990); Page, M. J. and
10 Sydenham, M. A., *Biotechnology* 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., *Biochem J.* 227:277-279 (1991); Bebbington et al., *Bio/Technology* 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a
15 chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No.209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., *Molecular and Cellular Biology*, 438-447 (March, 1985)) plus a fragment of the
20 CMV-enhancer (Boshart et al., *Cell* 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse
25 DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol
30 outlined in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the vector does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially
35 available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five μ g of the expression plasmid pC6 is cotransfected with 0.5 μ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 μ M, 2 μ M, 5 μ M, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 μ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

Example 9: Protein Fusions

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., *Nature* 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the halflife time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

5 For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that
10 the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a
15 heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

GGGATCCGGAGCCCAAATCTTCTGACAAACTCACACATGCCCACCGTGCC
CAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAACC
20 CAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGT
GGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAC
AGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG
AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAACCCCC
25 ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT
GTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCT
GACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGA
GAGCAATGGGCAGCCGGAGAACAACACTACAAGACCACGCCTCCCGTGCTGG
ACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCA
30 GGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGC
ACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGTGC
GACGGCCGCGACTCTAGAGGAT (SEQ ID NO:1)

Example 10: Production of an Antibody from a Polypeptide

35 The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) For example, cells expressing a polypeptide of the present invention is administered to an animal to induce the production of sera

containing polyclonal antibodies. In a preferred method, a preparation of the secreted protein is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

5 In the most preferred method, the antibodies of the present invention are monoclonal antibodies (or protein binding fragments thereof). Such monoclonal antibodies can be prepared using hybridoma technology. (Köhler et al., *Nature* 256:495 (1975); Köhler et al., *Eur. J. Immunol.* 6:511 (1976); Köhler et al., *Eur. J. Immunol.* 6:292 (1976); Hammerling et al., in: *Monoclonal Antibodies and T-Cell*
10 *Hybridomas*, Elsevier, N.Y., pp. 563-681 (1981).) In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at
15 about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

 The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line
20 (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (*Gastroenterology* 80:225-232 (1981).) The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide.

25 Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a
30 mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce formation of further protein-specific
35 antibodies.

It will be appreciated that Fab and F(ab')₂ and other fragments of the antibodies of the present invention may be used according to the methods disclosed herein. Such fragments are typically produced by proteolytic cleavage, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). Alternatively, secreted protein-binding fragments can be produced through the application of recombinant DNA technology or through synthetic chemistry.

For in vivo use of antibodies in humans, it may be preferable to use "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric antibodies are known in the art. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

Example 11: Production Of Secreted Protein For High-Throughput Screening Assays

The following protocol produces a supernatant containing a polypeptide to be tested. This supernatant can then be used in the Screening Assays described in Examples 13-20.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2×10^5 cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in

Examples 8 or 9, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a
 5 control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of
 10 cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37°C for 6 hours.

While cells are incubating, prepare appropriate media, either 1%BSA in DMEM
 15 with 1x penstrep, or CHO-5 media (116.6 mg/L of CaCl₂ (anhyd); 0.00130 mg/L CuSO₄·5H₂O; 0.050 mg/L of Fe(NO₃)₃·9H₂O; 0.417 mg/L of FeSO₄·7H₂O; 311.80 mg/L of KCl; 28.64 mg/L of MgCl₂; 48.84 mg/L of MgSO₄; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO₃; 62.50 mg/L of NaH₂PO₄·H₂O; 71.02 mg/L of Na₂HPO₄; .4320 mg/L of ZnSO₄·7H₂O; .002 mg/L of Arachidonic Acid; 1.022 mg/L of
 20 Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitic Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml
 25 of L-Asparagine-H₂O; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL-H₂O; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H₂O; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalanine; 40.0
 30 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-2H₂O; 99.65 mg/ml of L-Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319
 35 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; and 0.680 mg/L of Vitamin B₁₂; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine;

0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; and 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37°C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 13-20.

It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide directly (e.g., as a secreted protein) or by the polypeptide inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

Example 12: Construction of GAS Reporter Construct

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN- α , IFN- γ , and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:2)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

	<u>Ligand</u>	<u>tyk2</u>	<u>JAKs</u> <u>Jak1</u>	<u>Jak2</u>	<u>Jak3</u>	<u>STATS</u>	<u>GAS(elements) or ISRE</u>
<u>IFN family</u>							
5	IFN-a/B	+	+	-	-	1,2,3	ISRE
	IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
	Il-10	+	?	?	-	1,3	
<u>gp130 family</u>							
10	IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
	Il-11(Pleiotrohic)	?	+	?	?	1,3	
	OnM(Pleiotrohic)	?	+	+	?	1,3	
	LIF(Pleiotrohic)	?	+	+	?	1,3	
	CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
15	G-CSF(Pleiotrohic)	?	+	?	?	1,3	
	IL-12(Pleiotrohic)	+	-	+	+	1,3	
<u>g-C family</u>							
20	IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
	IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP >>Ly6)(IgH)
	IL-7 (lymphocytes)	-	+	-	+	5	GAS
	IL-9 (lymphocytes)	-	+	-	+	5	GAS
	IL-13 (lymphocyte)	-	+	?	?	6	GAS
	IL-15	?	+	?	+	5	GAS
25	<u>gp140 family</u>						
	IL-3 (myeloid)	-	-	+	-	5	GAS (IRF1>IFP>>Ly6)
	IL-5 (myeloid)	-	-	+	-	5	GAS
	GM-CSF (myeloid)	-	-	+	-	5	GAS
30	<u>Growth hormone family</u>						
	GH	?	-	+	-	5	
	PRL	?	+/-	+	-	1,3,5	
	EPO	?	-	+	-	5	GAS(B-CAS>IRF1=IFP>>Ly6)
35	<u>Receptor Tyrosine Kinases</u>						
	EGF	?	+	+	-	1,3	GAS (IRF1)
	PDGF	?	+	+	-	1,3	
	CSF-1	?	+	+	-	1,3	GAS (not IRF1)
40							

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 13-14, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

5':GCGCCTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCG
AAATGATTTCCTCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTGTCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATG
ATTTTCCTCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCC
CTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGC
CCCAITGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGC
CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT
TGCAAAAAGCTT:3' (SEQ ID NO:5)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 13-14.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 15 and 16. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

Example 13: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1% Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies)

with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final
5 concentration of 10^7 cells/ml. Then add 1ml of 1×10^7 cells in OPTI-MEM to T25 flask and incubate at 37°C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing a polypeptide as produced by the protocol described in Example 11.

10 On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

15 Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12
20 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples
25 from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20°C until SEAP assays are performed according to Example 17. The plates containing the remaining treated cells are placed at 4°C and serve as a source of material for repeating the assay on a specific well if desired.

30 As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

35 **Example 14: High-Throughput Screening Assay Identifying Myeloid Activity**

The following protocol is used to assess myeloid activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate myeloid cells. Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the
5 Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 12, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2×10^7 U937 cells and wash with
10 PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM
15 KCl, 375 uM $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 1 mM MgCl_2 , and 675 uM CaCl_2 . Incubate at 37°C for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37°C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400
20 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting 1×10^8 cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of 5×10^5 cells/ml. Plate 200 ul cells per well in the 96-
25 well plate (or 1×10^5 cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 11. Incubate at 37°C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the
30 protocol described in Example 17.

Example 15: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are
35 activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon

activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or
5 differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

10 The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

15 Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

20 To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker)
25 containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

30 Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

35 To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS

(Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count
5 the cell number and add more low serum medium to reach final cell density as 5×10^5 cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1×10^5 cells/well). Add 50 ul supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR
10 can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

Example 16: High-Throughput Screening Assay for T-cell Activity

15 NF- κ B (Nuclear Factor κ B) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF- κ B regulates the expression of genes involved in immune cell activation, control of apoptosis (NF-
20 κ B appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- κ B is retained in the cytoplasm with I- κ B (Inhibitor κ B). However, upon stimulation, I- κ B is phosphorylated and degraded, causing NF- κ B to shuttle to the nucleus, thereby activating transcription of target
25 genes. Target genes activated by NF- κ B include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF- κ B promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF- κ B would be useful in treating
30 diseases. For example, inhibitors of NF- κ B could be used to treat those diseases related to the acute or chronic activation of NF- κ B, such as rheumatoid arthritis.

To construct a vector containing the NF- κ B promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF- κ B binding site (GGGGACTTTCCC) (SEQ ID NO:8), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5 5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC
TTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:9)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

10 PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

15 5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCC
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCCA
TCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACT
AATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTC
20 CAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT:
3' (SEQ ID NO:10)

Next, replace the SV40 minimal promoter element present in the pSEAP2- promoter plasmid (Clontech) with this NF- κ B/SV40 fragment using XhoI and HindIII.

25 However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF- κ B/SV40/SEAP cassette is removed from the above NF- κ B/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the
30 NF- κ B/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF- κ B/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described

in Example 13. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

Example 17: Assay for SEAP Activity

5 As a reporter molecule for the assays described in Examples 13-16, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below:

10 Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 µl of 2.5x dilution buffer into Optiplates containing 35 µl of a supernatant. Seal the plates with a plastic sealer and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.

 Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 µl Assay Buffer and incubate at room
15 temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 µl Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

20 Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25
24	130	6.5
25	135	6.75
26	140	7
27	145	7.25

28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-3, used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-3 is made in 10% pluronic acid DMSO. To load the cells with fluo-3, 50 ul of 12 ug/ml fluo-3 is added to each well. The plate is

incubated at 37°C in a CO₂ incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10⁶ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-3 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10⁶ cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-3. The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca⁺⁺ concentration.

Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase (RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating

tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of activating the tyrosine kinase signal transduction pathways.

- Seed target cells (e.g., primary keratinocytes) at a density of approximately
- 5 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or
- 10 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are
- 15 used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

- To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20
- 20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na₃VO₄, 2 mM Na₄P₂O₇ and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for
- 25 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and
- 30 centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

- Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a
- 35 biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and

PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂⁺ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30°C for 2 min. Initiate the reaction by adding 10ul of the control enzyme or the filtered supernatant.

10 The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide.

15 Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

25 **Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity**

As a potential alternative and/or complement to the assay of protein tyrosine kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

35

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

Example 21: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR

products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7
5 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenin deoxy-uridine 5'-
10 triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and
15 propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and
20 chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated
25 disease.

Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is
30 a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with
35 specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10.

The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 23: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracisternally, intravaginally,

intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules.

Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., *Biopolymers* 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (R. Langer et al., *J. Biomed. Mater. Res.* 15:167-277 (1981), and R. Langer, *Chem. Tech.* 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., *Proc. Natl. Acad. Sci. USA* 82:3688-3692 (1985); Hwang et al., *Proc. Natl. Acad. Sci. USA* 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

Example 24: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 23.

Example 25: Method of Treating Increased Levels of the Polypeptide

Antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 23.

Example 26: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

5 The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the
10 presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

15 The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

20 Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media
25 from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

30 The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

35 It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

 The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other

disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties.

305

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM


(PCT Rule 13bis)

A. The indications made below relate to the microorganism referred to in the description on page <u>212</u> , line <u>N/A</u>	
B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input checked="" type="checkbox"/>	
Name of depositary institution American Type Culture Collection ("ATCC")	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 25 SEPTEMBER 1997	Accession Number 209299
C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/>	
D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States)	
E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable)	
The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications e.g., "Accession Number of Deposit")	
<div style="border: 1px solid black; padding: 5px;"><div style="text-align: center; font-size: small;">For receiving Office use only</div><div style="display: flex; justify-content: space-between; align-items: center;"><div><input checked="" type="checkbox"/> This sheet was received with the international application</div><div style="text-align: right;">Authorized officer Sonya Barnes PCT International Division</div></div></div>	<div style="border: 1px solid black; padding: 5px;"><div style="text-align: center; font-size: small;">For International Bureau use only</div><div style="display: flex; justify-content: space-between; align-items: center;"><div><input type="checkbox"/> This sheet was received by the International Bureau on:</div><div style="text-align: right;">Authorized officer</div></div></div>

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(PCT Rule 13bis)

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Date of deposit 25 SEPTEMBER 1997	Accession Number 209300
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Name of depositary institution American Type Culture Collection ("ATCC")	
Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America	
Date of deposit 02 OCTOBER 1997	Accession Number 209324
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308

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(PCT Rule 13bis)

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Date of deposit 09 OCTOBER 1997	Accession Number 209346
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What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:X;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.
5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
9. A recombinant host cell produced by the method of claim 8.
10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;
 - (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

- (g) a variant of SEQ ID NO:Y;
- (h) an allelic variant of SEQ ID NO:Y; or
- (i) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the secreted form or the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

- (a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

- (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and
- (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

- (a) contacting the polypeptide of claim 11 with a binding partner; and
- (b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

- (a) expressing SEQ ID NO:X in a cell;
- (b) isolating the supernatant;
- (c) detecting an activity in a biological assay; and
- (d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

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<151> 1997-10-24

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<212> DNA

<213> Homo sapiens

<400> 6

gcgctcgagg	aatgacagcg	atagaacccc	gg	32
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<210> 7

<211> 31

<212> DNA

<213> Homo sapiens

<400> 7

gcgaagcttc	gggactcccc	ggatccgctt	c	31
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<210> 8

<211> 12

<212> DNA

<213> Homo sapiens

<400> 8

ggggactttc	cc	12
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<210> 9

<211> 73

<212> DNA

<213> Homo sapiens

<400> 9

gcggcctcga	ggggactttc	ccgggggactt	tccgggggact	ttccggggact	ttccatcctg	60
ccatctcaat	tag					73

<210> 10

<211> 256

<212> DNA

<213> Homo sapiens

<400> 10

ctcgagggga	ctttcccgga	gactttccgg	ggactttccg	ggactttcca	tctgccatct	60
caattagtca	gcaaccatag	tcccgcccc	aactccgccc	atcccgcccc	taactccgcc	120
cagttccgcc	cattctccgc	cccattggctg	actaattttt	tttattttatg	cagaggccga	180
ggccgcctcg	gcctctgagc	tattccagaa	gtagtgagga	ggcttttttg	gaggccctagg	240

cttttgcaaa aagctt

256

<210> 11

<211> 826

<212> DNA

<213> Homo sapiens

<400> 11

ggcagcagaaa	tatatgggtct	tttctgattc	tatttatagg	aaatgtccag	aataggcaaa	60
tctacagaaa	cagaaaacta	gattgggtgat	cgcctagagc	ttggggcagg	gggtggggag	120
tgggtaatga	cttctaata	gtttcttttt	aagggtgatga	aaatgttgta	aaattgattg	180
tgattattgt	actaaaaacc	atttaacgta	tattaagggtg	ggttaattgt	atggcatgcg	240
atattatctt	caacaaagct	gtgagtgtgt	gcgcccattg	atggatgtgt	atgtgtgtgt	300
atatatctct	atacatgtat	acatggatgc	ccatgtgtat	ctatgtagaa	tatgtaaaac	360
aaacatgagg	tagtttgata	ttttagtctg	gagctacaga	gagatctaag	cccagcgatc	420
aagattcaga	aatcagcagt	cactgagggt	gtagtagcta	atgggattgt	ctaaaggaaa	480
tgagagggga	ggagaatggg	tttccacaga	caacctctct	tggaaactga	aaagaaatca	540
ctagacagaa	gggaatgaac	tagagaagac	tggctaactt	ggaggtcaag	tgtgagcttc	600
atcttctgcc	tgcgaggtgg	gaaacttatt	tctaactgat	tctctgggtt	tcaacacatc	660
ctctgggttc	tccagggcat	aggggagtg	tgtgtgtgca	ctgtgtcagt	ggggagtgga	720
agactgaata	aatattgcaa	atggaggga	cagccagagg	gtgcaaaggc	ctcgggagca	780
tgaggggaatg	cagctcacca	gcagagtctc	aagcagttca	ctatgt		826

<210> 12

<211> 524

<212> DNA

<213> Homo sapiens

<400> 12

gcacagaggg	cttgggtgca	ggtggtttat	ttgggaagtc	atcctggaaa	atccaaaagg	60
aagggatgga	gaagagatag	aagacaagaa	agaatgcatt	gctcgtgggt	catgggtata	120
gaaagtctct	aggaagcttc	tgcagaacct	tatgcaatgt	gcctcgaatt	gtccaaggaa	180
ttgaatgggg	agctgggtgca	tttgtacact	acttctgttg	ctcaactgatg	ggcaacaggg	240
cttttatccc	cagcctttcc	aggctgcccc	ggggagacag	cagctatggg	gaggcaccaa	300
cccatgggct	gtactcattc	cagaatcctt	ctcccttacc	acgtgacag	tcaattattc	360
accaagtgtg	aacttcgaat	tctacttacc	taaaatgcgt	ttggcataca	tctgcatgtc	420
acactcacac	tgccctatc	ttggctcgaga	cattataatc	actctcctga	actactgcag	480
cagcttccta	gctgaactcc	tggtctatct	ggtctatatt	gctg		524

<210> 13

<211> 491

<212> DNA

<213> Homo sapiens

<400> 13

ggcagcaggg	aaaagcttgt	gctgttagct	ttaaagtgtg	tttaaaataa	atctgaaatc	60
atctaaacag	catgaacctt	ggtggccaaa	tagatcaatg	acaaagagga	gaaaacctag	120
atacaggttc	atctttgcct	tatatgcttt	gagattagtg	tttctattta	gagctgtgac	180
taatacacag	gcacacaggc	tgagagcaaa	gcgaggtgaa	tgccctatt	aattgccacc	240
atgggtgcgag	gctggaatga	gggtgtggcc	agctaagagg	ggatttgctc	ttcttgcctt	300
agaagtctct	cattgtttcc	tgtctgtct	tgtgtccagc	tgcttagcac	acttctcttt	360
ggtattttaat	gctttttata	gctggaacct	tgaggttcct	cagaaatctg	cacatgctta	420
ctagatgggtg	ctctggattt	tctttaaaga	taggaagaaa	aaggcaaagg	caggtctgtg	480
acgtctctta	c					491

<210> 14
 <211> 403
 <212> DNA
 <213> Homo sapiens

<400> 14
 ggcacgagcg gggccctaga gagcaactcg aggtccaaac ccttcatect aaagaagggg 60
 acgctgcggc catgacattc catgcctccc aaggctctag agctataaaa tgggtggagcc 120
 atgactgagg gectgctgtc ttctctctca ttgttactgt atttattaac ctgggttactt 180
 atgcttttcca aaaagcttta tgtgcaaagt atcttttgcg ataateccaca ctccagtcag 240
 atggatgcat gcaatgggaa cagtcagaag atccacaatg ctagacagtg cacctgatgt 300
 gcagttcctg gaatggagct ctcttcccca aagcctaaatg tttctctctga aacctctgt 360
 tctttaacgc tgaagtccgt gatgcctgct aggagcagct cga 403

<210> 15
 <211> 813
 <212> DNA
 <213> Homo sapiens

<400> 15
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 ctgcttctgc tactgatcca aactgcagaa cttctcattc atccccaagg cctccaggca 120
 gtaaccaatg ggggaatcagc tctaaaagga accagaccaa cgttttccag ccccttcatt 180
 ctgggtgactg aggggaggaa agaatgggag ggggtattct tgtctagtgg atggaaagga 240
 aacacactgt caaattacta tatctccttg gttttctatt acagtagaat tctccagcca 300
 tatttttatt gtctatgggg gaagtgtggag atgggtgacct tgattagaag tgtctggagg 360
 gggataaatg gaggggataa gatttcagtt gtttttggaa aatgttaaaag tcttaaaata 420
 atgcgtccca tctgaagaat tttttctaaa accagagttt ataaaaatat cactgatata 480
 gcttgccccc tcatttccct gccacaggag atgtcttggg ctagagacac ttgtttaata 540
 atagcttgtc tctgatattc ccagtagctt cctctctgtg gaggaagga tagaaatgtt 600
 caggacatca tcatacagc cctccatctt caaagtctca gtacagtgga cgcctacacg 660
 gaagacttgg aactgcaaac aggcctgggt taccctcagtg acatctgacg ctgtccaacc 720
 agaagttcga tttttgttct gggggtgaag gaggaacag actgtactaa aggactaaaa 780
 taatttgtct atactaaaaa aaaaaaaaaa aaa 813

<210> 16
 <211> 264
 <212> DNA
 <213> Homo sapiens

<400> 16
 gtttaataata tgtgcagtggt attattaagt atgacattct cttttctctt agagttttgt 60
 tcagtggccc aaaggctaag attagcagat gtagaacat ctatgcagga tattttaaaa 120
 tgggttagtg actataacct gagggcagat ataagtaagt caagagattt atagggaaaag 180
 gatttctttg aagattgttg cagatgggct aatgaagga agctctcaat agctatccaa 240
 aacacctggc atgtttcttc tcga 264

<210> 17
 <211> 520
 <212> DNA
 <213> Homo sapiens

<400> 17
 gagaaggact ttatgcaggg aagtgcagca ggacacggag ggaactcatat ttaccgagct 60

BNSDOCID <WO 992243A1 I >

<213> Homo sapiens

<400> 19

ggcacgagga	agcgtgaacc	ccaggggaaca	gcggggtccct	ccccctccca	gacacaagcc	60
acctcagctt	gtgggtcttg	gccccagcc	ccaccaaccc	acctgttcat	ttattcaaca	120
gacaatgaca	gctgatattt	attggacatt	tgcaccatgc	caagcattcg	gcttggatta	180
ccccatttgt	ttctcacagc	cggtatttat	tgtctgctcc	tctgtgccag	gtgctgtgct	240
ctgggcaggg	gcactgcacg	ggctgcttgc	cttgggtggag	cttgtgggtc	gatgggtgag	300
gctgacccaa	gccccccca	ttgccaacag	ggccagggca	agagtacaca	caggggcctc	360
ataccatatt	tctaaatatt	taaaaagtta	tcaatcaagg	taacaactgt	taaataaaat	420
atgtttctatt	ctctactttt	gaaaaaaaaa	aaaaaaaaaa			459

<210> 20

<211> 555

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (48)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (50)

<223> n equals a,t,g, or c

<400> 20

agctccaccg	cgttggcgcc	cgctctagaa	cttagtggat	cccccggnon	tgccaggaat	60
tccgccacga	gcaaggtcac	agagctagaa	aaaggcagaa	ttgggacctt	taccacagaat	120
ttctaactct	agctctgtta	agctgggaca	ctggagaagg	agagggtttg	gtgtagtact	180
ctcttgagct	cggggtctta	gaagtccaca	tggggctgct	ggagtgggtga	ggggagatgg	240
aggtgggaag	aagggagaag	acccctatct	ccctattctc	tttcaatcag	agaggattcc	300
tcgacttatt	tacctgctg	tgatctctac	tgaagagaat	tctatgaccc	ccccaaatct	360
gcgattcact	ctgttccagt	tctgttactc	tttatatctg	gagctagaac	tgggcttcag	420
atcactgtca	caagaggtga	ccagagaatg	gtgcttgagt	tacttttttt	taataaaaagt	480
ttgctggcaa	gttctctgtg	gtgagttcct	gcttgtaaaa	gagaacccat	tcttactttct	540
ggagaaaaaa	ctcga					555

<210> 21

<211> 665

<212> DNA

<213> Homo sapiens

<400> 21

ggcacgagaa	actccagtta	atgccattta	ttttgcttct	tgtttgctta	acctccctgc	60
cttctagggg	ttataatgag	aagaaactaa	cagacaatat	tcagtgtgag	atttttcaag	120
ttctttatga	agaagccaca	gcctcctaca	aggaagaaat	cgtgcacag	ctgcccagta	180
ataaaccaga	agagctagaa	aataatgtag	atcagatctt	gaaatggatt	gagcagtgga	240
tcaaagatca	taactcttga	cttataaggc	tagctactta	ataatcaact	ttgttgatat	300
ctctgccgac	atcatagaaa	ttgttcaagt	gtcagtaaca	ctttattaaa	atcatgttgc	360
agaaccagca	ggtggatagt	atataggttt	atgcctgtgt	ttctttttct	catgagaaaag	420
ctaaacatga	aataataatga	atatagtaat	tattaaggga	ttgagacaaa	aactgtgatt	480
ttaatactta	aattgctaaa	gaataaataa	atctgacaaa	atgggtggat	atcttttaag	540
tttattacag	aaaaaaatgc	agatgatctc	ttaaaataaa	actaaagata	aagcaaaaaa	600
aaaaaaaaaa	aaaactcgtg	ggggggggcy	cggtacccaa	tcgccctatg	agtgagtcgt	660

attac

665

<210> 22
<211> 777
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (274)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (278)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (295)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (676)
<223> n equals a,t,g, or c

<400> 22
ggcagagctc aggtaagarg caaaattact agaatatcca ctctcactga aaatgagtaa 60
aaacctaaact tagatgaaaa tccttatctt gttcattttt attcctggcc ttttggttga 120
gaagaatggg ccagaccatg tgtgtgtgtg tatgtgtgtg cgtgtgtgtg tgtgtgcgca 180
cttgggttta tttatatgag ccggtaaaaa ttccgttcacc attaatatat gttaatattac 240
caacttctta aatgagaaca gtgagaattt tctncatngt taataataca ctggncagtg 300
catatatgca tcacgaagag aggattttcc cattgataat agatttccaa atacatcttc 360
ctgctttaag attttaatat atggatttat atataaaaaa tagttaagtc attggaaaag 420
caaaactgtca wccttctctt atttgagawc tcaactttag aaagtctatg ttctcaacta 480
cagaaaaataa ttttttagacc agctaacttt cagattttctg cagtgttat tttctccag 540
ttgagggttg gtttttgttt gtttgtttgt ttgtttgttt ttcttgatta aaaagtaaga 600
atacggccag gcgcgatagc tcatgccttt aatcccagca ttttgggagg ccgaggaggg 660
cagatcacct gaggtncagg agttcgagac cagcctggct aacatgggtga aaccagttt 720
ctactaaaaa aaaaaaaaaa aaacttcgag ggggggtccc ggtacctaatt cgtccct 777

<210> 23
<211> 540
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (341)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (378)
<223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (425)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (450)
 <223> n equals a,t,g, or c

<400> 23
 gaggatcccc acagggcccc tctgtagccc tggggagtcg gcagtgcctgg tctaggcccc 60
 ttaggagagg gggcaggggg gcagcagtag aaatgtggcg gggtcggact tgggtgttcc 120
 ggccgtcttt gtgtctrtgt tgggtatgtg gagtgtcatt cggctcttat gtcctcaccg 180
 gcttcagttc ctccatgtgt gttctctgcc caggctctgc ctggctgtcc cttgtgtatt 240
 ccattctgtc agcccggtgg tccatgtccag amcggsttcc ttctcgggam agcctgggtg 300
 catctggggc atctgttttg ttgggttggc tctgggtgca nccagaccca ggagtgggtg 360
 tctctgttcc ccgagcanct gtctctgggc tctgggtggg tgtgagtcga tctgacctgc 420
 tgganttggc cccaaccaag cccccccan cctctcttct ctctctctca atcttccctt 480
 tctcttccaa cccctccaaa tggatgggtt gagtgccttg ggttgagggg aagcaatggt 540

<210> 24
 <211> 484
 <212> DNA
 <213> Homo sapiens

<400> 24
 ggcacgaggt cgggggaccg agggatgtga ggcctggcta caactccagg acaggagggg 60
 gagaatgcaa ctccagcctgt cctctctgtg atttgtggta tgcactaacg ctgtctgcac 120
 acatgcagct accaaccaag ccagactggt ggggttctta aaggctctga ggcccgccca 180
 cagccccctt tgcccttagg ttgctttccc tcccagttgc ccgctcttg tatttgttgc 240
 tacttacaga atcttttagg ccaaagggtt gaggctgggg ccaagaatct ggtgagcaac 300
 aagtcactgg ctctgcccc tccacttttg acaggggtga cccgggggtg ggagacgggtg 360
 atccagacc cgtgttcacc tgtggggctg tccagtgcga tgagggtaaa gaacgagttg 420
 gtcccactgc tcatagttaa tccctgccac ttggcaccag gcatagcaca aagcaagccc 480
 tcga 484

<210> 25
 <211> 707
 <212> DNA
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (562)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (570)
 <223> n equals a,t,g, or c

<400> 25
 gggctgaccc acgctgccc ccaagcgctc ggtttctaca acccttagga acatcagaat 60
 catgtgtgtg tgggtgctta ttaaataaam sagttccttg agctcactcc cagtgcactgc 120

cagtctgatg	attagggggt	cagctaggac	ctagggtttgc	gaaagctccc	agctgatctc	180
atgcagccag	cctggctctg	gctctggckc	tgggagctgg	gttgggaact	agtctttggg	240
gctattctgc	tgawacttca	agatgggctc	tttgactccg	tcttgatttg	tcakcacttg	300
tattcaggtc	tgtttctccc	ctggattgta	aactccttga	tgtctgggtc	atctcagctc	360
atgagctgag	cttwcagtgg	gtgctcagtg	gaacagatgc	tgaatggagt	caggctgtag	420
ggaggccagc	gtgtgttggg	aagtggagaga	caaaaatcat	tttaaaaaga	atctttttgc	480
ccttcagttg	tgtttgccat	gagttaatgt	gatttactct	agtgggaaggc	agtgcagctt	540
aagtggaggt	cttgccctga	antggagccn	ggttatggat	cagcagagct	gccaaaagcg	600
ttttggggga	aatgtttctg	tgtcaccctc	agttgattga	actcaagttt	tcactcccg	660
ttaacaccac	gtggggggcca	ttctgacttc	tggggagtg	gtatgat		707

<210> 26

<211> 793

<212> DNA

<213> Homo sapiens

<400> 26

ggcacgagta	ccattttattg	agctctagac	atatactagg	cagtgtgcta	agacttgatg	60
tgtgcatgag	ctcacctaaa	agtctgggtc	tactattagc	tgtaatctgt	agggaagcta	120
cataacttcc	tcaagctatg	twttttctaac	taaaagacag	gtaccttaaa	gatcatctgc	180
tgttgctctc	cctttgacct	actaacagag	attacaggtt	attaagcaat	ataaaacaag	240
ggttattlaa	agactctgtt	tttwgctgca	ttcccytcaa	cacccccgag	ctccacaaat	300
cttaaaagtc	aatgctctta	gcctacttta	ttttggtaca	cacctcagaa	acgaacagaa	360
ctgtcaaaaca	cctgtgaagg	caaagatcag	ctctgttctg	ctctacacgg	cctctgcagc	420
agctagcagt	acttagctct	cagtagcacc	cactccaaca	gcaagttgtt	tagctgttcc	480
ttatacacac	gcacacacat	acgcacactc	acacacacac	agactctgaa	gcttccctgg	540
cctctccatc	taactacca	catecttaac	ttttgctgca	aaaactccta	actgggcttc	600
ccacttcaat	actttctcaa	ctcaaaaagc	caagtgttct	ttttaaacct	taaatcagaa	660
cacgccactc	ttctgcttca	gattccccaa	ggatttctac	gcacttcata	tctaaactac	720
ttacgatgac	ccaaggccct	actagatttg	gcctgcttac	tttccagcgg	cacgagagag	780
aactagtctc	gta					793

<210> 27

<211> 638

<212> DNA

<213> Homo sapiens

<400> 27

gataagaaat	tattttaaat	tttttatgaa	tattgttctc	caattttagcg	ttcttctctca	60
ttttgcttat	ttctctttta	ttatcttata	ttgggctggt	ttgttcagcc	aaacaatttg	120
tagcatgtct	gttttcaaag	taaaatagtg	atatatttaa	agttctaaat	gtgttcttta	180
tgtattttta	aaggagatgg	gtaaaataga	atgtatttct	ctttaccctg	atgacattcc	240
cgtgatatat	ttcaaataat	attttttgatt	gggtaagcca	gtaggaccaa	atccatgggtg	300
atcacagata	cagattcaca	aatgcataga	gagaatcata	aatagatgca	tatggaggag	360
tctgacagta	tagtgaaatt	ggtttcaagt	aatttgacac	attagaactt	tcaggcattc	420
acctgccagt	aatccttatt	agaaatagga	ttggaatatt	ggggtcacca	gctcaagacc	480
atttttttgt	gagagctgaa	caataaccaa	aagtcagagc	tataggaata	aaaatgaacc	540
tattccagtc	attagaactg	tttctctgaa	taagctcttt	cttctctctc	ttcataaaaa	600
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aactcgaa			638

<210> 28

<211> 528

<212> DNA

<213> Homo sapiens

<220>
 <221> SITE
 <222> (421)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (436)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (459)
 <223> n equals a,t,g, or c

<400> 28
 cttaaaaaat aaatactatc tttctctctg gcctctccat cctccagaca atcactgaat 60
 tacaatatatt gcttaacagt agattaatgt caattttctg gaattttata tgactgatat 120
 aacatgtttc ctcttttcat acctgagtag tctcctgagc cctattttatt tagatgttct 180
 tcttttttct ttattattat ttttatttca catagcaggg atgcataatt tgacattcat 240
 caatcatgat atatgagtag ttcattcttc ttatcttaga atatgacatg ctatggaaat 300
 cactgtatac gaattcatct gcttatggat atgtttattgc ttcttatttt tgtctgttag 360
 gaataaaaact gcttggttaag caaaaaaaaaa raaaraaaaa aactcgaggg ggggccccgaa 420
 ncccaattcg ccttanagtg gagtcgtatt acaaatcant ggccgctcgt ttacaacgct 480
 gtggactggg gaaaaacctg ggcggttaac cccaacttta aatcggcc 528

<210> 29
 <211> 919
 <212> DNA
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (380)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (432)
 <223> n equals a,t,g, or c

<400> 29
 gatcgttttt gccattgcag tgaccaacag gactgtggac ctcaqtaaag gctttcccta 60
 catcagcate tgcrgatcct tccccctca ragctgcate ttcagccagg tgctcaatat 120
 gggagctgct ctggcccgct ggatctgcat tgtccgttac caccagctcc gggactgggg 180
 cgtcagaagg tggcctaacc agctgatcct atggacgggt cttctgtgtg ccttgggcac 240
 ytcctgtgga ggcaatttac caggtgagac ccagtcggcg cccagggctc gtwmccggcc 300
 ggctstytgga aytacaactc ccagcatgcc ccgtggccat aggcctwawg tctcgggggc 360
 tggttcccgc ccgccccttcn tgggacttgt atttttctct ggccattggc ctggaccggc 420
 tggatccctt gntctctgag tggggcatta cgagcgaggg tgtttgtatg taggattcgt 480
 tgattccagg acgttgggat aattttctgc cagccctct cccagctta tttaatgatg 540
 aaattactgg tccaggcgca gtggctcatg cctgtaatte cagcactttg ggaggcggag 600
 gcaggcggat cgctgaggt gaggagtgtg agaccagcct ggccaaccaa catggtgaaa 660
 ccccgctct cctaaaatat gcaaaaatta gccgggcatg gtggcaggcg acttaatccc 720
 agctacgtgg gaggcagagg cgggagaatc atttgaacct gggagggtgga ggttgcaagt 780
 agccgagatc gagccattgc actcaaacct gggggataag agtgagactt ctctcaaaaa 840
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa actcgtaggg ggggkyccgg tacccaacgc 900

gccctatagt ggatgcgtg

919

<210> 30

<211> 864

<212> DNA

<213> Homo sapiens

<400> 30

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acattttcat	aaatgggttg	ttgggttttg	tttattttgt	tataccttgc	cttgccacatt	180
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gtccgtaaaa	tacagatatt	tgtctcttaa	tgaatatata	cattcctcta	tcattagatt	300
agattaaatg	agtgtatctt	ckgtaattta	taagttaawt	ggatttaaca	ttttgttgac	360
aaaacaccta	ggcaccagca	gttttgtgta	gcccatagtt	ttagtttgaa	gtagctagaa	420
tcctctagtg	tacagtttga	cgagtttcat	ctcacctatt	taggcttttt	ggtggtttga	480
tacttgacat	caaaaggaaa	gcacctcttt	tcttgagtga	cttcaaggat	gcattaagcc	540
tgcagtgcct	ggcctcgatt	cttttccctat	actgtgcctg	tatgtctcct	gtaatcactt	600
ttggaggggct	gcttggagaa	gctacagaag	gcagaatagt	gagtaaaaag	attggtagtg	660
gccaggcttt	tagctcttca	gaggcaagtg	tctgtatgca	tttgtctcac	tattcatact	720
tttatttgaa	gagtcctacc	acagcatgat	taacgtgacc	caaagcagac	tttccccaaa	780
ggtaattgct	gtggaaaaca	tggggaagcc	atttgaacag	aagatgcaca	gttgaggtaa	840
aaaaaaaaaa	aaaaaaaaactc	gwag				864

<210> 31

<211> 919

<212> DNA

<213> Homo sapiens

<400> 31

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ggccgtgagc	ctctctcctg	tttccagcct	gcaggtgccc	tgttgcctgt	cttcattcca	180
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cttccctggg	cacttgaggt	caggcttttg	cttttttgtc	acattgagcc	acatgccttt	300
gatacacagt	tgtagcaaaag	aaggggaggtg	atgaacttgg	ctcactttct	tttctgattc	360
ccctccctac	tcctctctgca	ctccccaccg	aaccccagat	atcttatagt	cctaaggctt	420
gtagaggatt	aaggaaaagga	attggagatg	ggtttttactt	agttcacaga	aaagctttct	480
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cagtgtcttg	ttcatgtgtc	ctgaccccg	gtccttgaat	ccccactttg	ctttgggatt	660
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ggatgccaaag	caggcttgg	tcaatggcta	aacctcttat	tgtattacag	tgtaatgctg	840
atctcagcct	ggtctcaatg	ccagagcaca	cagagacttg	aataaaaactg	ttataacgat	900
taaaaaaaaa	aaaaaaaaaa					919

<210> 32

<211> 956

<212> DNA

<213> Homo sapiens

<400> 32

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atttgtcaac	tctgcaagag	acaaggggtg	gtacagaaaa	tatcatttta	tctgaaggaa	180
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tgcgaataat	ccagagtttt	ccaaaccata	tatttgactc	cctttactga	ctgatatgca	300
aagtttgtgtt	taactatatg	gaaaattgtg	aatccttttc	tccaagtct	acacactcca	360
cttgcttttc	ccttctacct	tgaattcatg	tgcattcccc	cagttttctg	cctttgtaat	420
ggaggttcca	gttcttctgc	agccacagtt	gcaggaaaac	caattgtaat	cagcagctgc	480
cctgctgsta	aaagctatta	gtgcematgt	tgttaatgac	cgacccagtt	gaatgtgctg	540
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cgtatatcag	cacgttgaat	tgaataaatg	gggagggtta	gacatatcac	tacctttgag	720
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gatgagaagg	gtacagttag	gtttcttttc	agaactaaac	acatttagcag	taacctgcaa	900
aatcaatac	caattacttg	caagcaaggg	cctaaaaaaa	aaaaaaaaaa	actcga	956

<210> 33

<211> 566

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (400)

<223> n equals a,t,g, or c

<400> 33

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cagtgttcca	agcctcggtt	tcttcggttg	ttagagggag	catattgggt	ggagggagtg	180
aggactgttg	ggaggggggc	tcttgatcac	aggtcagctc	ttgctatgtg	ttggctgcaa	240
gggaggacag	gcaggagtgt	ggaccggaca	cgttcagttg	tccaccaggg	atgaggctgg	300
actgagactg	ctgcagcccc	gctgggttgg	tggggtgggg	cagargcagg	gggcgggtga	360
ggcagcctca	ggaagctgct	gcccctgaac	ccccggggan	gtcccccaat	ccctctccct	420
ccttggttca	tggccggggc	tccgtgtgga	aagggtcatt	tttagccctc	gctttttttg	480
gttaatgggc	ttttcgcggc	ttctctcttc	gaaggggcta	wttcaggagc	agacatcart	540
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<210> 34

<211> 1564

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (796)

<223> n equals a,t,g, or c

<400> 34

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ctgcattata	tttaatcacc	acaatattcc	ttaaagggtag	ttgctgtagt	tgcatcatt	180
gctttacaaa	tgggaaactg	tggcttagaa	agttcatcag	ttgttcccaa	ccctagctgc	240
ccatatttag	agtcacttgg	gaacctttta	aacttctcga	tggcgaacta	caccccagcc	300
cagttaaatc	acagttctct	aggtgggttc	caggeatcgg	cctttttttc	agttcctcat	360
gtgcggccaa	gtttgagaac	cagaggtcac	acaggtgcya	agtgyagagc	tgaccttcca	420
acccaggaag	gcgggtgcca	aaatcacacc	tggcaaaagt	caccatcagg	ttattcactg	480

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ggaatttgaa attatgctgt caagctactc tacagatgta cccctcagggt ttctcaagtt 540
cttttcateg aacttgccac agacttattt tcttcattca ggagtaaaga aatggggctc 560
ctgcttctca ttaccttgga gggattctcc cccactcacg tttatatctc ttttaagctc 560
tcatttgaag aegtttccact tatatcactt gcaccatggc atcatctgcc tagggttttc 720
tgtttatttt cacagagcat acacatcact gtgtattcta gaaacagctg taggctcgta 780
ttaacaaagt gataanaatc tggggctwtg aagacatgta ggatattagc taactgaact 840
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caaaaattct ctatgaatgg tggcacatgc ctgtagtctc aaataactaga gaggtgaaag 1440
caggagaatt gcttgaacct gggaggtgaa ggttgcatg agccgagatc atgctactgc 1500
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tcga 1564

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<210> 35
<211> 1035
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (522)
<223> n equals a,t,g, or c

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<400> 35
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gccttgtcta aaaaagatta accataaatg cgagggttca cctctggact ctcaagtctg 120
ttccactgat gtgtatgact gtctttattg tttctatta tcttttatg agattgttat 180
tcaggtgcag ccacaatagg agacactgga gaggtcagj aaaaaacaca gtttatcaca 240
caggtcctag agacgaggca tgctgtgcca tgccatgctg ggcacttgg ggaagacgct 300
aggggtggtta ggaggaggga argattaggt tactgccttc atcgaggttt ccttagggta 360
gggcagggcg aacagtttag tttgaataat tttggcatac ttttagactgg cggggtggtc 420
tcgttgcttg gcacttggct ctgggatgat aggttagagga gtagtgcctc ttggggtata 480
agggccagat agaggagata tggctctgga ttttgaatag cntgscatat taaagacata 540
ctcctagctg ggcccyttgt tatctttaag aattggctag accttgaggg gacagtttct 600
caaatagcta gaaaggttct ttaacatgtt aaacatcagt atacaagaaa agctaaaagt 660
ccatctgtgc cagtgcata ctgtctkgct tactgtagca gtgtggttaag ttttgaaatt 720
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tcgggagggt gaggtcagga gaatcacttg aaccaggag gggaggttg cagtgaagtc 960
gagattgagc cactaacctc cagcgtggcg acagagcgag atccgtctca aaaaaaaaaa 1020
aaaaaaaaac tcgta 1035

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<210> 36
<211> 620
<212> DNA
<213> Homo sapiens

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<400> 36

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ctgagaggag	atgagtggct	gcaagtggag	gaagaacatt	acctacttca	gattttatgc	120
ctcttgctct	gaaacgaggt	cagcttttcc	ttatcccttg	gcttttcccc	cagggagttt	180
gcccgttgga	aggtgaacaa	cttggctctg	gaaaggaagg	actttctcag	tttggcattg	240
cctcttgccc	cagagtttat	ccggaacatt	cgctctcttg	gaaggagacc	caatctgcaa	300
caggttacag	aaaatctgat	taaaaagtac	ggcactcatt	tcttactttc	tgccaccctt	360
ggaggttaagc	aacatcacaa	tcccaagcta	attgggttgc	agaccattgg	aaataacggt	420
aagactcgtg	tagcgtagct	ccaacagtct	tatcttcttc	cgggcctttt	attgcctgag	480
aagtctttct	ggtgcatttg	aaaacagtgc	agtctcttca	catctcaatt	taccccgaaa	540
catctctatt	taattattcc	ctgaggaggg	gaagttgggt	atggcggttg	gaggtggaca	600
ggctcctaaa	aaaaactcga					620

<210> 37

<211> 973

<212> DNA

<213> Homo sapiens

<400> 37

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caaccacat	tacagatgta	acttagtgag	agaaaacatc	tccctgtttt	ccttcataata	180
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ttgacctcct	gtactaaata	ccacgccaca	tcagtttttag	ttgcctttct	tttttccctta	300
ggctagtttt	ttggtatacc	atttctaaac	caatggtagg	aacattttta	ggcatctttt	360
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gtcacaaaagc	tgcaaaccgk	tttaataatt	attaaagttt	taatttttta	atggattttg	540
gtcatctaag	tccgaaatg	aaatacacca	aacttggtct	tacttttgcca	aattgtccta	600
ctgtttctca	gaatcaacat	tttttagacat	tatgtagaaa	cactttttta	cctagttgts	660
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atgtggctcag	tagtgcatct	tgtgtgacca	ggcaagttct	gcagaacctc	ttctgaacac	780
cttcacctgt	gtaaaatccc	aggcattagt	taatctccaa	ccactatggc	aggatatgca	840
tctgagagca	aagaggcaaa	tggcaagcag	ajatacacia	ggtgcaagag	ctagagtagt	900
gatagaacca	gtgccaggac	gatctaaatt	cccttgcatc	gtcaataacrc	aaaaaaaaaa	960
aaaaaaaaact	cga					973

<210> 38

<211> 838

<212> DNA

<213> Homo sapiens

<400> 38

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atatctcata	taagtggaaat	cataaggat	ttgtcttttt	gtgattggct	tatttcattt	120
agcataatgt	cctcaagggt	cattcatggt	gttgcatgta	atagaatttc	ccttcttttt	180
aagggtgaat	aatatttcat	tttgtgtgtt	gagaggtagg	acctttaaaa	tgattatgtc	240
atgagggtct	tgccctcgtg	aatgaattaa	tgacattacc	atgggagtg	gttccctgata	300
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tattgcttca	cagctagtct	ctatagtttt	gtttttttaag	agatgaggtt	tcactccagc	780
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<210> 39
<211> 607
<212> DNA
<213> Homo sapiens

<400> 39
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caggcctcac tggcttcata ggtcttgagg ttgtagccca gttgttcaac tgtatggttg 180
gactactgtt aatagcactc ctcacctggg gctacatcag gtattcttgt caatatcgtg 240
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tcggtaattc cactcaggcc actgtgaggg atgcagttgt tggagacca tccatggata 360
aaaaagctca atagcatctt aacgtgaaga tcaacaaga acacaacaag cccctactga 420
tttctgggtt tctgccacgg ccacaggttc atatccagag gaatggcaga tctgagacga 480
tccaggaaga gctaaaacat ggccctgtaa taaatgagca gacctctct gtgggttcaa 540
attattaaac acacttccat ttctcttgga aaaaaaaaaa aaaaaaaaaa aaaaaaggg 600
cggccgc 607

<210> 40
<211> 882
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (198)
<223> n equals a,t,g, or c

<400> 40
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tgccgacctat gcccgcgggc gtgcccattgt ccacctacct gaaaatgttc gcagccagtc 180
tcttgcccat gtgcgcangg gcagaagtgg tgcacaggta ctaccgaccg gacctgatga 240
gaaacagggtt gagaagagtg aagttgattt ctcaaagcca catagcttta gtgagacgat 300
tlgaggatct gaagcccaag ctttctgttt gcmaaactgg gatcacaagt ctttcggtcg 360
gagaactgga agtctgggca gactcgagca gaggagacct gatgactgac tagacttgtg 420
ctcagtgtctg tgttggggag aactgctacg acatacctga aattccacca aagcgtggag 480
aactcaaaac ggagcttttg ggactgaaag aaagaaaaaa caaacctcaa gtttctcaac 540
aggaggaact taaataacta tgccaagaat tctgtgaata atataagtc taaatatgta 600
tttcttaatt tattgcatca aactacttgt ccttaagcac ttagtctaata gctaactgca 660
agaggagggtg ctcagtggat gtttagccga tacgttgaaa ttttaattacg gtttgattga 720
tatttcttga aaaccgccaa agcacatatc atcaaaccat ttcattgaata tggtttgga 780
gatgtttagt cttgaatata atgcgaaata gaattattgt aagtcacta tatgggttgt 840
ctttatttca tataaattaa gaaattattt aaaaaaaaaa aa 882

<210> 41
<211> 959
<212> DNA
<213> Homo sapiens

<400> 41
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caaaatgaag cttctccttt gggcctgcat tgtatgtgtt gcttttgcaa ggaagagacg 120
gttccccctt attgggtgagg atgacaatga cgatgggtcac ccacttcac catctctgaa 180

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aactttctct	ggattccccc	atgtctatca	catccgtggt	tttcccttag	ctactcagtt	360
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tgtacagcc	aagcctgctg	ccccagaacc	tcacctctct	ccctctcttg	aacaggcaaa	720
tcagtgaat	tctctagaag	agtaccatgg	gttcatttct	atactgatgc	agaaataagt	780
gaaatctaca	aaagttttct	ttcttttcca	aagactatct	cattctgttg	tattcagagt	840
attcatctca	ctacattgat	ttgtttgtgg	tagtttttcc	tgggacttaa	tttatattga	900
aaaaacattg	ataattaaat	aaataaaata	gataatttag	acaaaaaaa	aaaaaaaaa	959

<210> 42

<211> 875

<212> DNA

<213> Homo sapiens

<400> 42

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ccatccacgc	accacctcca	ggacgagaac	ccttgatgtc	aaaaccaagt	gcccagtggg	180
ggcgggtgaag	ctctcggaag	tgtgtccacc	tgtgtgaggg	cgggtctgaa	ctcgagggag	240
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cacccctgcc	tgtgggatgt	tgtgagagga	acatgagcca	gacaaagact	tggctcaggg	420
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agcaggccgc	tgaacaaaca	ccccagaagc	cagcactgtg	gcagggtgct	ggggagatgc	540
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tctgtggagg	tgaggagggg	agattccgtt	cacatcccag	gaggggcaaa	atgactgatg	720
tatttttatg	tattacaca	gagagtgcac	tttctctcca	gagatgetgt	ctgggttaaca	780
aaggaataac	ttaagaaatt	gattgattat	cttaataaac	tgtgcaaac	caamrrraaa	840
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaac	cgtag			875

<210> 43

<211> 630

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (26)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (29)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (56)

<223> n equals a,t,g, or c

<400> 43

ccctccctta	aggggaccaa	agctgnagnt	ccaccgcggt	ggcggcgct	tagaantagt	60
ggacccccgg	gctgcggaat	cggcacgaga	aacactgagt	tcagctgcc	tgtctagata	120
ttctggatta	ctacagcagc	cttctagcct	atgggtggaa	cccatctgat	acttttccca	180
ttcttgctta	gaacaatggt	gatatttctc	tgtttaaaat	cctcttggtg	ctcttttttg	240
cccattaata	aaattcaaac	tccatttata	cttaattctc	tatacaaaac	cttcaagatg	300
tgctccttac	ctaaactctc	tttttcccc	ttatcttcca	tatttttcat	ttttttctct	360
acctaaccct	gtagccttat	ctctcttctc	ggatgatctt	ttgttctacc	aatacccagc	420
ttctggaatg	ctagtgtttg	tttactcagt	cctccatttc	ctcttccctg	aattctagcc	480
tctcttctct	cccctaatac	agtatactcc	tactggctct	tcagaactca	gttttaggtta	540
taattctcca	aaaaattaca	attaggttct	ctctctggat	cccatccctc	aaaaaaaaaa	600
aaaaaaaaact	cgaggggggg	gccggtaacc				630

<210> 44

<211> 571

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (460)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (494)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (562)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (566)

<223> n equals a,t,g, or c

<400> 44

gcaacatcgt	ccttactcct	gcatttttct	gacgggcatg	ctcccacgca	gcttgcgcaa	60
caccaagcgg	gcgggtcaaac	tctcggtctc	attgttataa	gatcacataa	caaaaactttc	120
atcctggagc	tctctcatgc	gccgtttgct	gctcgctttg	ccgtttgcc	tgtctgcaact	180
ggctgtcgct	catgctcacg	aagaccatga	ccacgagcac	ggcagcctcg	gcgcccctga	240
acatggcgct	gggcgcctga	atgccgtgct	ggacgggccag	gccttgagag	tggaaactgga	300
cagcccggcc	atgaacctgg	tgggttttga	gcattgtagc	accagcgccg	ccgacaaagc	360
caaggtcgcc	gccgtgcgca	aacagctgga	aaatccatcg	ggcctgttcc	aacctgcccc	420
aagccgcagt	tgtgtgggtc	gcaaccaagg	aatcaacagn	cgttggttct	gacaaaccgg	480
aagccgagca	tgangacgat	gaccaagcct	ccgacgggaa	aaggcgccgg	cggcccacaa	540
agcatgatca	agacaaaaat	gnaatncacg	c			571

<210> 45

<211> 930

<212> DNA

<213> Homo sapiens

<400> 45

ggacaaaatt	gacccatttt	caataaatgt	ttataaccag	gggctgttac	tgctttgttt	60
tttttttyct	agctcacaaat	tgtaaagcag	cgagaacaac	cagaaatggt	tttccgacag	120
ttcctggtag	aagacaaaagg	actttacgga	ggctcttctt	atgtggattt	cctttgttgt	180
gttcacaagg	agatctgtca	gctgcttaat	taattgaaac	ttctctgtca	ttgatgttgc	240
atttccaagg	agataatctc	cttcttggtg	cctaattttc	tagatgataa	taggctagtt	300
ttgattttct	gctcattttc	agaataactt	tcaggaaga	gatggcattt	agaacttcag	360
ctttggtgct	caggtataaa	gccaattaag	gtacaattgt	accataaagg	gaacaatctg	420
ttcttgattg	cacagttttc	aattttttaa	actgatgtgg	tttgcatttc	ataaaaggca	480
aagtttacag	aaccataaac	attctcaatt	ttctttatgc	tagacatata	aattattttt	540
caaactgtat	agattttggg	taaaaagttg	tctcagttcc	tctcccaatt	gcaatgagaa	600
aaaaaagctt	aattttttaca	ttataacttaa	ttttctaaaa	ccatgtaact	ccattgaaca	660
cattttttcaa	cttaaggtct	gcatagcaga	cttttaataa	ccttgggatt	tatctggtag	720
aacaatatgt	gttctacatt	tttttcataa	ttatatattg	tgtatgttaa	aactattttc	780
cagttgtttt	gtctgtaaaa	ctgtctttat	caatatgctt	aatggttctt	tgtacaattt	840
tgaaagtttc	tacctgtata	taatggatgt	taaccagtat	caataaatca	ttcgtataat	900
cttaaaaaaa	aaaaaaaaaa	aaactcgtag				930

<310> 46

<311> 437

<312> DNA

<313> Homo sapiens

<400> 46

gcttccggac	gccaacatcc	gggccgcgcg	gggaagggga	gacgtggggg	agagtqacca	60
tgacgaaatt	agcgcagtgg	ctttggggac	tagegatcct	gggctccacc	tggggtggccc	120
tgaccacggg	agccttgggc	ctggagctgc	ccttgctcctg	ccaggaagtc	ctgtggccac	180
tgcccgccta	cttgctgggtg	tccgccggct	gctatgccct	gggcactgtg	ggctatcgtg	240
tgggcacttt	tcatgactgc	gaggacgccg	cacgcgagct	gcagagccag	atacaggagg	300
cccagaccga	cttagcccg	aggggstgcg	cttctgacag	cctaacccca	ttcctgtgcg	360
gacagccctt	cctcccatct	cccattaaag	agccagttta	ttttctaaaa	aaaaaaaaaa	420
aaaaaaaaaa	aaaaaaa					437

<310> 47

<311> 1024

<312> DNA

<313> Homo sapiens

<320>

<321> SITE

<322> (5)

<323> n equals a,t,g, or c

<320>

<321> SITE

<322> (14)

<323> n equals a,t,g, or c

<320>

<321> SITE

<322> (32)

<323> n equals a,t,g, or c

<320>

<321> SITE

<322> (713)

<323> n equals a,t,g, or c

<400> 47

gtggntcccc	cggntggcca	ggattcgcca	cngggcgctg	gccgccttcc	agctgctcaa	60
cctgactggg	caacgtgggg	ctcttctctg	gctcggatcc	cagcatccgt	ggcgtgatgc	120
tggccggccg	cggctctggg	cagggctgag	cttactgcta	ccaatgccaa	agccagggtg	180
cgccacgcag	cggacactgc	tctgcttggc	gcgtctgcat	cctgcgtcgg	gaccaccact	240
gccgmctgct	gggcccgtgc	gtgggcttct	gcaactaccg	gcccttctct	tgcctgctgc	300
ttcatgccc	cggcgtctct	ctccacgtct	ctgtgctgct	gggccctgca	ctgtcggccc	360
tgtctgcgag	ccacacgccc	ctccacatgg	ctgccctctc	cctgcttccc	tggtctatgt	420
tgtcacagg	cagagtgtct	ctggcacagt	ttgccttggc	cttcgtgacg	gacacgtgag	480
tggcgggtgc	gctgctgtgc	ggggctkggc	tgtctttcca	tgggatgctg	ctgctgcggg	540
gccagaccac	atgggagtg	gctcggggcc	agcactccta	tgcctgggt	ccctgccaca	600
acctgcaggc	agccctgggg	ccccgctggg	ccctcgtctg	gctctggccc	ttcctggcct	660
ccccattgcc	tggggatggg	atcaccttcc	agaccacagc	agatgtggga	canacagcct	720
cctgactcca	ggaagagcca	gagctgtgca	gggaggaagg	ggtgagaggg	gggccccccac	780
acctagactc	agtaaggaag	tggggttggg	ccttaacatc	tgcattggac	aactccaccc	840
cttcttggc	cttgcctctg	cccgcttaca	ctcctacgtg	tccagggtct	gggcctgac	900
ttaggcagag	gagtgacag	gagggctctg	caggggctgc	tccaggccgc	tagctgcccc	960
tttgccaggt	taataaagca	ctgaattgtt	aaaaaaaaaa	aaaaaaaaaa	aaagggcggc	1020
cgct						1024

<210> 48

<211> 463

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (14)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (462)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (463)

<223> n equals a,t,g, or c

<400> 48

gaattcggca	cganttacag	gcattgagca	ccgtctccgt	ccttgactgg	tgattttcta	60
ctgaaaccca	gacatgttag	gtattacgag	actctgggtc	ttactgaaac	cttgcttccc	120
acgtctgtac	tccagcacag	gaggggaggt	gctgcgcgt	tgtgtgagg	tggaggcgga	180
agtcagggtt	ccccactcag	cacccatgga	ctctagagaa	gggggcactg	tgccttactt	240
tggaggggtg	gggagtccta	gatttacta	gaccagcact	ggctgtgagg	ggtggggggtg	300
tcaccttact	gctctttcat	ggcctccact	ttcaccatat	tctcaggatg	gcagtgcact	360
tggagtgagg	agaggggatg	tgattgggca	ggagacgcag	gaggcttcaa	aaaaaaaaaa	420
aaaaaaaaaa	aaaaaaactc	ggggggggcc	cggaaccaat	tnn		463

<210> 49

<211> 885

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (233)

<223> n equals a,t,g, or c

<400> 49

aattcggcac	gagagggctg	cataccttgcg	ttctgtgagc	tctgcccgtt	gggagcatcc	60
atgctgatgt	gcaggggccc	tgcagcactg	cattctctctt	gccttctctg	ttctgttttag	120
tacaaccacc	ccagcaggte	tccagttcct	gccaggtttag	tgtggatggc	ccagcaccat	180
ctcctctcca	tcttgtttggc	tatcctctct	tgttctctac	aaccccgcca	ggntcggggc	240
tcaggagctc	tgcctgttga	agtgtgtctc	gcagttctcc	tcacatgtct	acgcaaaatc	300
tctggctccc	tgtgtgtctg	agcccaacag	acacactgag	cacaggagtt	ggctctcagc	360
tcctcccagc	ttgccgtgac	tgagccytgc	cgctctgtgg	camcgccasg	gagaccacag	420
tgtccaactg	tccaaccttt	acgttaattgg	catcccagga	ggagaagcaa	gagtgaatgg	480
ggcaggaaaa	gatacattaaa	gaaatcgtgg	ctgacataaa	aaaggatgag	ttcatgtcct	540
ttgtagggag	gcgtggatga	agctggaaac	catcattctg	agcaaaactat	cgcaaggaca	600
gaaaaccaaa	caccatgtgt	tctcaactcat	aggtgggaat	tgaacaatga	gatacattgg	660
acacaggggtg	gggaacatca	cacacggggg	cctgtcgtgg	ggtgaggggg	atggggcagg	720
gatagcatta	ggagatatac	ctaattgtaa	tgacgagtta	atgggtgtca	gcacaccaac	780
atggcacatg	tatacatatg	taacaaacct	gcattgttgt	cacatgtacc	ccagaactta	840
aattataata	aattaaaaat	aaaaaaaaaa	aaaaaaaaact	cgtag		885

<210> 50

<211> 847

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (337)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (407)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (415)

<223> n equals a,t,g, or c

<400> 50

ggcacgagtg	aaaccataaa	gaaaaccaag	gggggtgataa	atataaaatc	caacgtgggtt	60
attacctggt	tacgggcagg	actatgatag	ggaagtcact	ggttatgttc	tgtttcctaa	120
gctggggggc	aggggtacat	gggtgtgcac	tttattataa	tgtttccaac	cgtataggta	180
tattttatat	attctgtttt	acatatttga	gattgcataa	atgtgtaatg	ctcagtaact	240
taagagtaaa	tgaactgtga	agaatttagag	atggagtttt	gagggatttt	ttgttttggg	300
ttgatttttg	gagaccagat	cctggctttg	cggctcangct	gggaatgcag	tgatgtttatc	360
catggcctca	cttcagcctt	tacctctctg	gggctcaggt	gatacctncca	acttncgggc	420
ttcgattagc	tggggacttc	aggtgcacac	caccacaccc	agttgacttt	taaaatttttc	480
gtggagatga	gttctccctg	tgtattgccc	cacgctgggc	tcaaattcct	ggcttatgga	540
atcctccctg	agccagggtc	ctggccagtt	tttgggttgt	tttgtttttc	tttttttgaga	600
tggcaatttc	gctttattgc	ctcaggctgg	agtgcagtg	cgcgatctcg	gctcactgca	660
acctccatct	cccaggtaaa	agcgattctc	ctgcctcagc	tactggggaa	gctgaggcag	720
gagaatcaat	tgaacccayg	aggcggaggt	tgcagtgagc	caagatcacg	ccactggact	780
ccagtcctga	gcaacagagc	caagactccg	tctcaaaaaa	gaaaaagaaa	aaaaaaaaaa	840

aaaaaaa

847

<210> 51
<211> 580
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (557)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (569)
<223> n equals a,t,g, or c

<400> 51
caagaaaagtt tgcatttata acacaagtaa cacatgttaa gtccctctttt acaatctctg 60
ttagttgcac tcaatgttct ttttctcttc ccaaaacttct tagcaatttt taaaaacctg 120
acctacgatt gttatttttag gttcttccca attttttttc tgccctccca ggaaatgtgg 180
tatctctgac ttccacagct ctcaatttga tcataaacac caagggttct tccccctgga 240
gtgggagaca caatagggat ggggatgtgg gagaagaag aggattctat gaatatccat 300
agttttattt caccaccccc aaatgtattt atattaaagg acccaactgaa gagcgctggg 360
gagatggtag actcttgtct gaagtcctta tctacacca atataatctt cttcttaggc 420
cttctccac taggtgaaag gggataagct tggggacatc tagaaagggg cattaatttc 480
cccaatccta tgagctacat ttgagactca cagtattaga aagccggggg tttatcacag 540
ctcttttggg agaagcnaaa ttttttttng gacagcttct 580

<210> 52
<211> 598
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (515)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (523)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (558)
<223> n equals a,t,g, or c

<400> 52
ggcacgaggg tggcggggca gggcggggct gcatgcgatg acgtcgatgt gtccggccgc 60
ggcgctggcc tggcgacact cggcgatttc ctgatcgtc agcctggcgc ccagctgggc 120
cgcggcgcgc gacaactggg ccgcgtcgcc atacaccacg caggcgcgc cagccctgcg 180
cgcagccttg acgacgattt cggggccgat gccggcgcca tcgcccatgg tgatgcccac 240
gggcagggag gggttcacgg tgcctgggaat gggattgcgt tcgggataat gctacacccg 300
ttcgcggggc acggccgggc ttactgcttg ccgtttttcg gcggttcgat gacgcgcgat 360

tcgaagggtga	ccgtgggcgcg	cctggggagcc	caagccgggtg	gcgttggttg	gagtgatctc	420
cggtttgaag	cagcttgcg	tcccatggat	ttcgcaatgc	tgcttcgcgc	gcttgcaacg	480
cctgggttct	tcagcttcca	acccaagttc	agcancttgg	ctncccgga	gcttttaagt	540
ttaacctggt	aaagtgtnc	cttggttcgaa	ccttggttg	aaccttcggc	ttcaatgc	598

<210> 53
 <211> 571
 <212> DNA
 <213> Homo sapiens

<400> 53	
gaattcggca	cgagtcaccac
caaaatgatg	agcatttttc
ttttaaatct	tttttaact
taaatgtttt	taattgtgtt
atattctata	gaagtctgct
tggttggaat	tttggttttc
ttttgtgcat	atgcagcctg
ttacttaaat	ctgtttttat
tctattctcg	tacatttttc
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	aaaaaaaaaa a
	60
	120
	180
	240
	300
	360
	420
	480
	540
	571

<210> 54
 <211> 1247
 <212> DNA
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (2)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (9)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (1131)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (1202)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (1209)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (1226)
 <223> n equals a,t,g, or c

<400> 54

cnccacanc	cacaaattgg	tttgggttgg	tgtaagtcag	gcttcccacc	aaagtccaat	60
atcttctaca	ctctagtgc	ataaaaaatta	ttattaaata	gctaagaggt	gtgcatgtgg	120
gaaaggtcag	tgcatatccc	tttagggagg	gagaatgttg	taatatatca	gctatcgagt	180
tgtttaaaaa	aagtgtatyc	aaycgtatat	tgtctatagt	atgtgctatg	aaatttgc	240
ttatgatatg	taacaggggc	aaagccaaat	tcatgttact	ctgttcagtc	agaaacattt	300
tgtggcatatc	agcattcctg	ggaagtgctg	tactttgttt	cgttttgggt	ttagttttgc	360
atcttagagt	ccttataatt	gatgcctatt	ttaatagcat	ttcttttttag	cttttgggtc	420
gtattttccat	tcactgttcg	tatctgttac	tttctattaa	agcattatct	gtttaccaca	480
tgtacaaaaa	ctctttgaat	aatatgcatt	cctagttttc	agccaagtcg	gggatgttag	540
tgattgtacc	agcccmaagc	acttggataa	tcagggccct	tcttcccttt	ataatcaatc	600
atcaacatca	gaaaaagcta	cttgttttat	ttatatcccc	ttccaaatcc	gctctggaac	660
atgcagtaac	tgacacaaac	ttatttttag	aacaaatata	attggcaact	ttggaatata	720
tttgatattc	cattaggatt	tttctaaaaa	gggaaataaa	ctatatatat	atatgtatct	780
tacccccaat	tcttccaaca	gaattttctat	aggaagccat	ggatgatggc	ataagtgttc	840
cacatattac	atgattttta	ataatcctca	aaatacccaa	ggaactctta	aagagtgttg	900
gtatgagtat	actacttttg	tttaatttta	gcttcatgga	tgttctgcat	ggaaggattt	960
ttgtttttcca	cattttccca	ttgttagcag	agtgaatccc	aagagaccaa	acatttgcaa	1020
gcattgtatt	tgagcacttt	tgtaaaaaaa	aaagaaaaaa	aaaaaaagga	aaatatatat	1080
aatacttaaa	aaaaaggtat	ctaggaagg	ctaccctcag	gattggggac	ntctcttaac	1140
cctacctccg	ggaccccg	ggagggatgt	tggccctatg	tgggggtctg	tttattccat	1200
tnnttttctc	tttaggttg	gtatctttt	tgggggggtt	ttttccc		1247

<210> 55

<211> 848

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (8)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (15)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (98)

<223> n equals a,t,g, or c

<400> 55

cccccaanga	acagnttttg	gtaaatccaa	aaattatgcc	acttttataaa	aaaaaaaaaca	60
aaccttataaa	cagggatctt	aataccctcc	ccttggtntc	cccttgcttt	actcctccac	120
tttagaatat	tttcttataa	aatcacctca	aaggactgtg	aggaaaaggct	gtgggtacctg	180
accttggtga	aatcaaggcc	cggcaactgt	ctacaggcct	gtttacagat	tattacgggtg	240
aactgaatgg	gtaccgaggc	ttcaccaaag	aggtaacttt	ttgttggttg	tggtgtttta	300
ggaataattg	taccaatttt	aagagcatte	ccccacctg	ttcccacaca	cccaaacaaa	360
atgtgggtgg	gttgccctca	aaaaagagaa	gttttggtgc	attaacatga	cagaagaact	420
ttttaaaaaa	aaataactgt	caactattct	atttgcattt	aggagactgt	tmatctatgc	480
tagattgtca	tttccctcc	ttctccaca	gaagtttact	ggtagtccat	gtcatggctc	540
gtagctatcc	ctctaaccat	accatggaaa	tgcaggcacc	caatgtgaaa	aggagcactt	600
gctgggcatc	actgacaccg	ctcatgtttt	acacatagtt	gagtaatcag	catatctaga	660
attatctttg	attgcctaaa	tcatatgtat	atagtgaatg	ttatataata	tacctggcag	720

gtctgttttta	atttaattga	acaaagatac	aaataactttg	tttggtctggc	aaatattaaa	780
ttatttatatg	aaaaaaaaa	aaaaaaaaa	aaaaaaaaa	aaaaaaaaa	aaaaaaaggg	840
cggcgcgt						845

<210> 56
 <211> 669
 <212> DNA
 <213> Homo sapiens

<400> 56						
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ttaatcacct	tgaagatccc	ttaagaggca	tttgactggg	gctgcgcgtct	gtgtccctcaa	120
agcaatgctg	gtggcatcgt	cctgtgtaca	catgcagagc	taatacccaa	actaaaaact	180
gggttaactgg	ccctgaagtg	cttcccaatc	agtaagccac	agggaaatgt	ttgattttta	240
tgtttctgttg	gattttgggt	tgtttggcat	atctaaagggt	gccttttactt	ttcttttttt	300
ttttttttct	ttctgctttg	ttttgttagga	cttggttctaa	catggaaaac	aagtccagaa	360
gactctctct	tgaactgtta	ctttgccccca	agccaccccc	aactttttatg	ctcatgtttt	420
attaaagcag	gtgctccctg	gaatctcttg	gacatttttg	aggcatttga	agcagaatat	480
agagtgggtc	catctccttc	cttaattcttc	ctgggtgggtg	ggatgttcca	cttgatcat	540
agattttttt	attacagata	tgttccactg	tttttaaatg	tgaacttctg	cgcacatgtg	600
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aaactcgag						665

<210> 57
 <211> 680
 <212> DNA
 <213> Homo sapiens

<400> 57						
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tctgtccacc	gtccttggtc	ccgtagtatc	accgggtgct	tttttactaa	atgagagtat	180
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tgtttatttt	aactctgggt	ctaattcatg	tgcaggtcag	cttgccaaga	aacacttaag	300
gctctgtttt	ctgcatgtag	gcaggtaatc	ctctgataga	gaaacataga	gttatcccat	360
caaaatgtga	gcacagaaat	gtatcaacaa	catgccataa	gccagtcgat	atatctaaaa	420
gccaaactgt	aaacgggtcc	ctgtgcccc	gaaagggtgt	cagaatatac	ttgttttttg	480
aggtttttaa	attaattggc	actagacaca	cccagctgaa	gcaagggtct	tcgtctgggtt	540
tgagcttctc	ctgcttttta	ctgatgctaa	aatgttttaa	tttggtcttg	gtagatttta	600
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ctaaaaaaaa	aaaaaaaaa					680

<210> 58
 <211> 524
 <212> DNA
 <213> Homo sapiens

<400> 58						
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aaaagggaac	attgattctt	taagctttta	atcaaacatg	tgggtcagtc	acatttgaaa	240
tgttagttca	aaatattaac	atatagttat	gttggttgatg	tcaactgaaat	tttaattgtgt	300
aaaagcagca	ctgtgcattc	tttaaagtaa	taaattaatg	gagttattgt	taaaacagag	360
tattctttttg	acaacattaa	atattttctg	gagaaagttc	acttttccag	tggctcaaaa	420

atttgttttta ggtcccgaga ttttaagtgg tatattaacc aataa...at attttggctg 480
tcaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaagggcgg ccgc 524

<210> 59
<211> 427
<212> DNA
<213> Homo sapiens

<400> 59
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taaggtaaga atcaaatagg agaaagcctt agctgttcca gcggcccatg tttaaaagaa 180
tgtgtcttctt ttccaagta tttctgcgc ttgcatgcac tgagcttctt tggaaaggag 240
caccatgcag gcataattttc cagacaggac tggatttget cgttactcag aggtgtgtgc 300
attcttttget tttaggatat ttaattagca tcttttaata gtgatattac ggtgtcttaa 360
aagtttatgc atttgaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 420
aaaaaaa 427

<210> 60
<211> 1263
<212> DNA
<213> Homo sapiens

<400> 60
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gaagccgggg acaggatgaa agcaacaaca cttttgcaga cagtcgaccg gcccaaggac 180
tgggtacaaga cgatgtttta gcaaattcac atgggtgcaca agccggatga tgacacagac 240
atgtataata ctcccttata atacaatgca ggtctgtaca acccaccta cagtgtcag 300
tcacaccctg ctgcaaagac ccaaacctac agacctctt ccaaaagcca ctccgacaac 360
agccccaatg cttttaagga tgcgtctctc ccagtgcctc cccacatgt tccacctcca 420
gtcccgcgc ttcgaaccaag agatcggctc tcaacagaaa agcatgactg ggatcctcca 480
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taatttatatg caaacaaaaa tatctataca ctttaagaaga accacttgc tctctgaage 720
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catcagataa ttcatacatg atatttgtct aagccttctt acccttctct taaataactc 1200
atatctttta gagtaacagg actacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260
aaa 1263

<210> 61
<211> 720
<212> DNA
<213> Homo sapiens

<400> 61
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ctacattggg aaattgaagg aattgctaaa tgctgaattc agcaaccagt ttgagattgt 120

tgaaaataaa	gattgtttct	tccaatgc	aagttcacag	atcactggag	tagctac	180
agtttgttct	agaccagagg	ttgcagatat	ttttgtccta	taaagagaca	catgggtaat	240
atTTTTggt	ttgtgagctg	tatagttttc	gttgtagctg	ttcagctctg	ctacatgaag	300
caaccataga	ccatacctta	acaagtgggc	acttttgagt	accaataaaa	ctttatttag	360
aaataacaga	gggctggatt	tggtcctagt	ttgctgaacc	cttttctaga	tgaaggctcc	420
tcttgccaag	actggctccc	taccttggt	gacaaaattct	cactttggga	cttagtcatt	480
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ttttttctta	catttaattt	aacaatcatt	actgagcgt	ggtagtctta	gtttcttttc	600
tcttcttttc	tccttttctt	ttcttttttt	ctttttcttt	atttgaaggc	tctcactctg	660
tcactccagc	ctgggtggca	gaccaggacc	ctgtctctaa	aaaaaaaaaa	aaaaaaaaaa	720

<210> 62

<211> 589

<212> DNA

<213> Homo sapiens

<400> 62

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tgggcaacgt	ggttqqaatg	tatctggctc	agaactatga	tataccaaac	ctggcraaaa	180
aacttgaaga	aattaaaaag	gacttggatg	ccaagaagaa	accccttagt	gcattgagact	240
gctccagca	ctgccttcag	gatatactga	ttctactgct	cttgagggcc	tcgtttacta	300
tctgaaccaa	aagcttttgt	ttctgtctcc	agcctcagca	cttctcttct	ttgctagacc	360
ctgtgttttt	tgttttaaaag	caagcaaaaat	ggggccccc	tttgagaact	acccgacatt	420
tccaacatac	tcacctcttc	ccataatccc	tttccaactg	catgggaggt	tctaagactg	480
gaattatggt	gctagattag	taaacatgac	ttttaaaaaa	aaaaaaaaaa	aaaaaaaaaa	540
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaag	ggcggccgc		589

<210> 63

<211> 686

<212> DNA

<213> Homo sapiens

<400> 63

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gccacgggat	gggggtggggg	agccccatgg	gcctgggaag	gaggggtgctg	tggagggggc	120
tgcagggctg	accagcaggg	agcctcatct	ggtcgggggc	gggggcggca	ggagcagaag	180
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ggctagaagc	ccccatggct	tctggcagct	ggacatcagc	cccaggatatt	gggggtgattt	420
tggtcatgac	agtgtgcctg	tcccactgtt	acacgcattg	atgggggtta	tgggggtggg	480
gtgggactca	agccttgacc	gactcctagt	ggacctgatg	tgaaattcct	gtcaaaacaa	540
caccactttt	caatgggtttg	ctaggagtat	ttctgtattg	aaagtttcta	attatgcttt	600
ttaaaaaaat	actaaaaata	aaggttcaag	ctgccaaaaa	aaaaaaaaaa	aaaaaaaaaa	660
aaaaaaaaaa	aaaaaaaaaa	aaaaaa				686

<210> 64

<211> 452

<212> DNA

<213> Homo sapiens

<400> 64

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ctgcttcaag	gtcagttaca	ctacttctgt	ggatgggccc	ttctctggct	taagcttggc	120

tgtccctggc	tttcccaagg	atcacagccc	aaaaggcaca	gtgggaaaa	tttatggcct	180
attcgagaag	agtgagcagc	ctaatacaagc	caagccttga	tttgggggttc	tcacttcact	240
ggatattttcc	ctctgtccct	aattgggttt	tctatagtta	ctagttttcc	aggcctccaa	300
gggagattct	gaggcttgat	gtgttctgac	tgtgtcttgg	ctttgtgatg	ctgagtgcc	360
gaaatactct	gtactataaa	aactaccatc	gttctttgaa	acaacaaaga	ggaataaaga	420
acttaattct	ggtgaaaaaa	aaaaaaaaaa	aa			452

<210> 65

<211> 370

<212> DNA

<213> Homo sapiens

<400> 65

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acagcctagt	gttaacattc	ttggtatctt	tttgtgcctt	atctaaaaca	tttctcgatc	120
actggtttca	gatgttcatt	tattatattc	ttttcaaaga	ttcagagatt	ggcttttgtc	180
atccactatt	gtatgttttg	tttcattgac	ctctagtgat	accttgatct	ttcccacttt	240
ctgttttcgg	attggagaag	atgtaccctt	tttgtcaact	cttactttta	tcagatgatc	300
aactcacgta	tttggtatctt	tattttgttt	ctcaataaaa	tattttaagg	taaaaaaaaa	360
aaaaaaaaaa						370

<210> 66

<211> 987

<212> DNA

<213> Homo sapiens

<400> 66

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ttgtcttcta	ggatcaactc	ggtcattacc	acagctcaaa	cctgctttgg	gactccctcc	120
cacaaaactg	gtctcggatc	agggaaacact	accaaaccaa	cagcagtaaa	atcagggtctt	180
tcctttctta	agtctgatac	cattaacaca	gatgctcaca	ctggggccag	atctgcatct	240
gttaaatcct	gctgcaggaa	tgacacctgg	taccagagac	caccatttga	ccctgggagg	300
gttgaatgta	caacagcaac	tgacaccaca	tgtgttacca	atttttgtca	cacaacttgg	360
agcccagggc	actatcctaa	gctcagagga	attgccacaa	atcttcacga	gcctcatcat	420
ccattccttg	ttcccgggar	gcctcctgcc	caccagtcag	gcargggcta	atccagatgt	480
ccargatggr	agccttccag	caggaggagc	agggtgtaaa	cctgccaccc	agggaaacccc	540
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tcctttatcat	tgattatatt	atggaataga	ttgagacaca	ttggatagtc	ttagaagaaa	780
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aatcccaact	tttaaaaaa	ataattcaat	ggataaatct	gtctttgaaa	tataacatta	900
tgctgcctgg	atgatatgca	tattaaaaa	tattttggaaa	actgaaaaaa	aaaaaaaaaa	960
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<210> 67

<211> 1018

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (1014)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (1015)

<223> n equals a,t,g, or c

<400> 67

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tcttgcccca	gatgattgag	aagaagcgga	aaaaagaaaa	ctctagaagt	ctggatgtcg	240
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ttctcttgga	ccgcctcgtc	tttgcccggg	cttctctcat	gttggtcttc	ctcatcatga	420
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cggcgctgag	gatgaactgg	cggggtgtga	cgccactaca	gttcatcaac	atcaactacg	540
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aaaatttagt	cgaggcagtt	tcaattgtta	ctgtggacgg	aattaggatc	acaataaacg	900
ataatgcagg	ttcttcaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	960
aaaaaaaaaa	actcgagggg	gggcccgtac	ccaatcgccc	tgatgatgat	ctgnncac	1018

<210> 68

<211> 762

<212> DNA

<213> Homo sapiens

<400> 68

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tggcaggaat	gcctacataa	cagggaaaaa	tctattgatg	caagcagcgt	ggttccatat	180
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<210> 69

<211> 630

<212> DNA

<213> Homo sapiens

<400> 69

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gggtcttctg	aatggaaagt	agcatatatg	tgttttaaaa	atattaatcc	ttttgaaaag	360

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ggggacctgt	ctcaggtctc	tatatggtta	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	600
aaaaaaagg	cggccgctct	agaggatccc				630

<210> 70

<211> 940

<212> DNA

<213> Homo sapiens

<400> 70

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cctgtccccc	ggggtgacaa	ccttgagctg	ggagggcgag	cccctcagtg	ccttctttta	900
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<210> 71

<211> 1103

<212> DNA

<213> Homo sapiens

<400> 71

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ctgatcatcc	cattgtactg	caaaaaccag	aaaacaacca	aagtttttaag	tagcatttta	180
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<210> 72
 <211> 899
 <212> DNA
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (20)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (85)
 <223> n equals a,t,g, or c

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 tttcctcggg atgttttttc ttaggctggg ttcctttaca agctgcaatt atgttccatc 180
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 catataactt atccaaggcc acaaaaactag taataaacag agtgaaattc aacccaaaaa 780
 caaactacaa atccaaattt ctttacctct atgctgtctg tacttgctgt tactagcaaa 840
 gttctcttgg tgggagttac cccatccct ctccaaaaaa aaaaaaaaaa aactcgtag 899

<210> 73
 <211> 549
 <212> DNA
 <213> Homo sapiens

<400> 73
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 aaaaaaaaaa 549

<210> 74
 <211> 590
 <212> DNA
 <213> Homo sapiens

<400> 74
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aagtggaaatg	aaactatcaa	tcttacrcat	acagctttgt	tgaaaatgtg	gacttttagt	480
gagaagaaac	aaatgttaat	acatttagcc	aagaaatcca	caagtaaagt	actcttatga	540
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<210> 75

<211> 1056

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (1051)

<223> n equals a,t,g, or c

<400> 75

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aacctcccta	ggctacctga	ttatactggg	ggctctccatc	tttcccttct	gggtgcgact	240
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caaatgctgg	aagcctcgac	ccttatccat	ttacatcctc	ctcgcccggg	ttttcctgct	360
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<210> 76

<211> 930

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (919)

<223> n equals a,t,g, or c

<400> 76

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<210> 77

<211> 4463

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (3308)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (3469)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (4119)

<223> n equals a,t,g, or c

<400> 77

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<210> 78

<211> 791

<212> DNA

<213> Homo sapiens

<400> 78

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gtgaccattc	gaagtctgaa	atgcgggggg	ggagtttcat	ttttaagtga	agaccaaag	720
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<210> 79

<211> 1292

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (488)

<223> n equals a,t,g, or c

<400> 79

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<210> 80

<211> 1283

<212> DNA

<213> Homo sapiens

<220>

<221> SITE
<222> (341)
<223> n equals a,t,g, or c

<400> 80

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tttata	tttta	ctactg	caga	aaattat	tttg	attcttt	tttc	agagaaa	ata	ctgttt	gggt	120
atatttt	ggg	gggagt	tttg	aatttc	acat	acgaaa	gaaa	taacac	agcc	ctttc	aaact	180
gcctgt	gttt	caacct	gcaa	agtttt	tttt	gtgcta	aaaga	tttgag	cttt	gtga	aggatt	240
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ggagtct	ctt	cctcyt	ctga	gccwac	aaaag	ctcggg	tcca	cgggt	actct	gscaaa	aatte	420
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gatatg	taaa	tagatt	tggga	tacga	atttat	tgtata	tacg	aagga	aagagt	gccaa	agcct	1080
acatacc	acg	ctttta	aatag	ttttta	aatct	tcgtt	atttaa	agaaa	agattg	agggag	atgg	1140
gatttt	ctgtt	tttatt	ttttat	acaaat	ctgc	attgtt	tggaa	tttttt	ttttt	tttac	gaca	1200
agctgt	tatt	tctct	gggga	gtttaa	aaaaa	aataca	aaaaa	aaagga	gaatt	cgatat	caag	1260
cttatc	gata	ccgtc	gacct	cga								1283

<210> 81
<211> 708
<212> DNA
<213> Homo sapiens

<220>

<221> SITE
<222> (40)
<223> n equals a,t,g, or c

<400> 81

aggcc	aggcc	tccac	agacc	ccc	atggccc	ccagg	gacgn	agggg	aggac	agagc	cccttc	60
agaac	agagg	ctc	atctca	ctg	catcccc	catc	accccc	tagtt	cccca	atggt	cctaa	120
tttgt	gttct	gagat	cccag	ttt	actccgt	ggcc	agggcc	caoct	gtgtt	tcca	agtcgg	180
gctgg	agacg	caggat	gggg	tagg	ccttgt	gctct	gagca	acccc	agctc	tgcc	tacag	240
gcagg	caggc	ccggt	gcaag	agt	ggactct	gggtt	cctaa	agca	ataaat	gcaa	acaagc	300
caac	agctct	gctgc	ctagc	aattt	ccatc	ttag	ccacac	ttct	cccttc	agggg	cttcg	360
gagg	agaggt	cagg	gctaag	gcc	ggggatg	agact	gcagg	agag	agagca	gcgg	agggcc	420
acatt	cggag	cctc	cgcca	ctcc	agtttt	atcag	ctttt	gcctt	tttgca	cggag	tgcta	480
aacaa	attct	agct	ctgtgt	ttttt	ttccca	ttccc	agatt	tact	atcagt	tctc	cttaaa	540
aagt	atctaa	gctgt	tacag	tagc	tttccc	ttcact	tgat	tctat	tgtgt	gtttt	ctatg	600
tttgg	aataa	ttac	acccaa	atat	ctagat	atttt	ctctt	cacc	gcattt	tgtaa	ataaa	660
gagat	gtgta	tgcc	aaaaaaa	aaaaa	aaaaa	aaaaa	aaagg	gccc	ccgc			708

<210> 82
<211> 1464
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (15)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (63)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (132)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (887)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (889)
<223> n equals a,t,g, or c

<400> 82
gactgtgctt gcagnaagag taaacactct cggatgccgc tgtcctgggg gagcccgcg 60
gangctgtga atgttgatac gagctggcca gtcctgggccc cagctcactt gtccagctac 120
ctgccagggtg gntttcactg tgttttaaaat acattgcatt ccaagctggt cccctctgtg 180
tatcactcta ctgagaaatc ctgcctagtg tgttttggga tgtgtcctag catttacaag 240
aaaatgaaaa gcgtccctctt aattggcacc cgaatgttgc tgtggctcag tcacatatcc 300
gagggccctc gtcccggaggc cgtgctgccc cgagcccccga gcccctctgc agctcaccct 360
tggtctgttt tccgcaaacc cggtaaacgc aagcccttgg ggcagatgca gaagcagaag 420
agggaggggga aacctgcctc tgggtcaccc tgttagcaca gcgttctcat cgggagacag 480
catggaactc tctctcgagc tgctcgaggc tgtgtgtcag tgtttgctgg gcttgtggct 540
ccttttttgg ctggataaaag aagtcgctgt ttttgtactg cttctgtggc tcttcacaga 600
cctcacggat gtgaccggag atgagtgccg atgaccacgt tttaaaggag aaagagagct 660
cctgggtgggg ccttcgggggt ggtctcaggc cacatttgca gtctgcaaca gtgacgcgca 720
cccggtccag agcgtgggtga gctttgtttg ccttctgggt cggctttcgc tgtgtctcct 780
gtgtgtgtta gaatccagag ccagaggaa gtgcaagcgg gtccctccgc aacggggaga 840
gcctctctgc ggcgctgttg gcgacamagc gctgtgaatt cgcgtanang gggagtgtt 900
tgaaacacct tcttgagttag tccggccttg tcaatgagt cttgttttcc tttaaacagt 960
ctgacatatt tactcgtcac tttcaaacca gaagcatgaa aggaaggaga tattgtgggg 1020
tccgttttaac tccatagaaa gcgcaggggg atggcccccgc gcgcaggctc ttgaccgct 1080
cagcgttgac cccaccgccc tggccgaggc acttggcctt gctgagctgg acttctctct 1140
cctctctctc atgaccgggg tgaattagaa cgttttttaa gacacccctc tccaaattct 1200
gtaacacatt gtaattggag aagaaggaaa ctctgcaagg ctaaactgtc attcacaact 1260
tggtctacaca tagactctag tcagttttgt ctccagaacc ttaggctttt gtatttttta 1320
atttttaatt cactgttaat ccttattgtc ttttttatta agatgttgga aaagcaggag 1380
gtagtgtgtc ctcaattatt gcaaaaatgt aacaataaag ttcctcaaaa taaaaaaaaa 1440
aaaaaaaaaa aaaaaaaaaa aat 1464

<210> 83
<211> 616
<212> DNA
<213> Homo sapiens

<400> 83

tcgacccacg	cgctccggtea	aaatagtggg	aaattagtag	aaataacata	ttttatatcc	60
aatttagtct	ccaaaatccc	aacatgcact	cttctgtata	cgtttttcag	tatgcttgac	120
tggaaacggc	aattctacag	tagtcttgga	agcaacatac	tcagagattaa	ataccttagt	180
agcctatgtt	cttgaatgag	gacataaagg	agcaatgctt	ttcttatctt	aaaaaaacag	240
tttatatgaa	tgaaccttct	gttctgttta	agatattata	tgttggtgag	tgtagttgtc	300
aaagcaacta	gcacgattcc	aagtaatata	gaaatcacca	gcttgagttg	ggtctgccat	360
aacagcacct	aaaacgtatc	cactaaatta	gtattaaatg	gacaagtaaa	ccaaactcag	420
agggttgaaa	tgaagacttg	taatacccag	tgaaaaaaaaa	ttattgaaac	taccatctaa	480
aattaattgg	aagcttaata	ttacctctag	gaaagagtgt	gggaaatgag	gaaagggcaa	540
aaggtaatgt	gttccagttt	gttctgttcc	ataatcccag	gaaatagata	aacaccaggc	600
aaaaaaaaaa	aaaaaa					616

<210> 84

<211> 928

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (916)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (917)

<223> n equals a,t,g, or c

<400> 84

aaaacaaaag	gagacgaagg	acgcatgcgt	ttgggtgagtc	ccggattctg	gtgggttctt	60
ccgctcaggc	tgggtgaagc	gcttccgggt	cgcgcgcggc	agcagcctcc	cggcgcgatg	120
aagacactga	ggctcagaga	ggttaagtga	ctcagccaag	gtcaaacagc	tagtaagtgg	180
tggagccagg	actcaaagcc	agtctaggag	ccatgtccac	tttggtcccc	tcactcttcc	240
ctcgtgtgac	tgagactctg	tggtttaatc	tggatcgacc	ctgtgtggaa	gagacagagc	300
tgcagcagca	ggaacagcag	catcaggcct	ggctccaaaag	catcgcggag	aaagacaaca	360
acctgggttc	tattggcaag	ccagcctcag	agcactatga	tgacgaggaa	gaagaggatg	420
atgaagatga	tgaggatagt	gaagaggact	cagaggatga	tgaggatatg	caggacatgg	480
acgagatgaa	tgactacaat	gagtcaccgg	atgatggaga	ggtcaatgag	gtggacatgg	540
aaggcaacga	acaggatcag	gaccagtggg	tgatctaggt	agacaaggca	gggtggcctc	600
agggagattc	caggccagcc	caaactaccc	tgcaccccaa	cccccaaccc	ctgcccacag	660
aaccagctga	tggccccagt	gcctgaaaag	gcccttgggc	acctcctcag	ctgctgccag	720
gatctgggtc	ctttggcccc	tcccaggcca	tcagtctgca	cttgaaatcc	ccagggcctg	780
aaacctactc	caccttctct	gccagtacct	cacctcttga	ttgccaggtc	tggctctaagt	840
ttctttaata	aagacaaaag	agtgattttc	caaaaaaaaa	aaaaaaaaaa	aaaaaaactc	900
ggggggggcc	cggaannaat	ttccccca				928

<210> 85

<211> 723

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (722)

<223> n equals a,t,g, or c

<400> 85

tattgtagtt	agaaccatct	gacacatagc	ttttattcca	ttgggttttt	gttatgtctt	60
tctttacaag	aatttgaagt	ccatcaggcc	gggagttttg	tttgttgtgt	ttgctgctat	120
ctcccagtgc	ctaaaattgc	ctggcataca	gtaggcattt	aataatcttt	gaatcagtga	180
aaaccagatg	gtggcttggc	atttccacat	aggaatgagc	cagggtggaaa	tcattccagga	240
tataagtaga	tcttgaagtg	ataaggaagg	gtcatcataa	tcattgtggg	cccattttgc	300
cctttcttgt	ttcttttctc	taggctcagc	aacagcctca	ccaaggactc	catgaatata	360
aaagcccata	tccacatgtt	gctagaggtg	agagcagctc	accccactac	cagactctgt	420
gtttagggtg	gtgacctgaa	gaagggaagag	agcgaaagaa	gggaaggacc	atctttccct	480
ctaaactgga	gtcaagggag	ggaggtcaga	gcaagcctgg	gggcgtaacc	cagaccctgt	540
ccttggtcaa	tctcttctgt	cctctttttc	aggggcttag	agaactacaa	ggcctgcaga	600
atttcccaga	gaagcctcac	cattgacttc	ttccccccat	cctcagacat	taaagagcct	660
gaatgccttt	gaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	720
ang						723

<210> 86

<211> 570

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (6)

<223> n equals a,t,g, or c

<400> 86

gaattncgca	cgagctcgtg	ccgtttcatt	ctgttttagaa	gttcatgttc	atcttagcca	60
tttggaactt	cttcattctc	tatcttttct	ccacgggtggc	tgggcttgtc	tgcaaatcat	120
tgtgtcaaaa	tcaaaactatt	ttcaaaacag	cccttttgctt	ctgagccctt	cccctaagtc	180
ctctgtgggg	gtccatgatt	ctgcagaggt	atgggacaga	atcttcagat	tttacccttt	240
gagtctcttc	ctagtcatat	cctggttccc	tcattctaat	attgacaaag	gatgactcat	300
taagtgcac	tggttatgta	actttcaaat	actttcattg	tgtatgtcag	gatctgagga	360
acaaaatgat	gtcatttaat	cggaatctaa	atgtgacaca	aacaacgtgc	cagcaatacc	420
tgcttgtgaa	ataatgttct	gagcccacag	tgttcctggg	tatgtgagtt	tatatcaagt	480
gaaaaggctg	cttaattgac	attaaagttt	tgggaatgtaa	agcttcaaaa	aaaaaaaaaa	540
aaaaaaaaaa	aaaaaaaaaa	aaactcgtag				570

<210> 87

<211> 639

<212> DNA

<213> Homo sapiens

<400> 87

gaaaaaatgc	tagggagaca	aatcaaatg	ttaaggggct	gggctctcag	cacattcttg	60
gtttgcattc	tccagtgggt	cagaagcctg	acaatccgcc	tagcctctgc	tttgagcgtc	120
aggggaccca	gttctattcc	tgcatectta	gccatcatct	acacactttt	tatcttttct	180
tttaaatttt	taaaaattgt	gaaatctata	tacatataag	ccatatgttc	aacttaaaga	240
atagtaaaca	actgtgtccc	taggatccaa	gttaagaaat	agatcagagt	cagtttctta	300
gaagcttcta	tatgtgtctc	tccccagtc	tgtgtctctc	tgtctctacc	tgagggaaat	360
tacagatttc	atgcttttct	ttatagtttt	cctttacaca	cataccctta	agcctctaag	420
tactatatgg	ttcggttttg	caaagcccag	aagcctattt	taatgctgta	tataagaata	480
tgctagccgg	gtatggtgac	tcatacctgt	aatcccagca	ctttcagagg	ctgtggcagg	540
agggttgctg	aagcctagga	attcaagacc	agcctgggca	atataggagg	accccttcac	600
tacaaaataa	aaaattaaaa	aaaaaaaaaa	agggcgggcc			639

<210> 88
<211> 708
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> n equals a,t,g, or c

<400> 88
tacggacacg aggnccgaaaa tgagaaaggt aacaatttcg aaaaagcatg cccctctgct 60
gtgtttccag ttgttttagat gtctgctctc catgtatata tggatcacat tcgtgttaga 120
tggaagttgt ggaatccact gttctctcaa accggtctct tcccttgta cctatcatag 180
tgtacatagc tcaacttcct gagtttgatt ctagtgttca aagataggta tttttcatat 240
aagatgtcct gtcaaagcaa gtcattgaac ttacctggtt tttaactgaa aacaaacaaa 300
aatcagcaat ctcttcatt gcttgtagaa atactgactt aggccaggca cagtggctca 360
cgtctaattc cagcactttg agaggccaag gcaggagtat catttgagcc caggagtctg 420
agaccagcct ggcaacatag tgagaccttg tctctgtaaa aaggaaggaa ggaaggggaag 480
gagggagggg tggagccaga ggaggggagg ggacactctg ttatacttat cgaaagggtgc 540
tatccaggtg tggtagtgca gccgatagtc tcagctactc aggaggctga ggtgggagga 600
tcacttgagc tcaggagttt gaggctgcag tgagctatga tggtagcatg tactccagcc 660
tgggcaacag agacagacca gactcctaaa aaaaaaaaaa aaaaaaaa 708

<210> 89
<211> 949
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (508)
<223> n equals a,t,g, or c

<400> 89
catgataacc ccaactcgaa taaccttcac taaagggaca aaagctggag ctcnccgcg 60
gtgccgcgcg tctagaatta gtggatcccc cgggctgcag gaattcgscg cgaggttggt 120
tgtgtgtgtt gcttgggtgt ttgtctcctt tgtaatggct gtgggtgaca agtgtgtcag 180
agtacttgtc cctcctatat gtgtatctat gcgcacgtat ctttctttgt gtgtctgctg 240
ctgtatttgt gtctcttctt agcgagtggc tgcaggatat tgtgccctcg ggggtgttct 300
tctggtgcca tggtagagt actatctggt tctcttggtt ttcccttggt tagctttcag 360
tgtgttttct ggatttttct tttgcaacga tagtaagcgt actctgcatt cctgtgcttt 420
gtgtttgtgt gcaggatat gctttcccta tatgtttctt ttctgacttg atttgtgact 480
agctgtgtgt gtacacggct gtgtgcanc atttgctgaa atgcagttgt gtgtgtgtgt 540
gtgtgtgaga gagagagaga gaggagagag agagagaagg agactatggc ttttctgttt 600
gkmcaaarrr catgtsagcc tatgagtgcc tctctctgtg actggagctg tatgtggtta 660
catgtggtca caagtgcaca ttcaagttca catacacaga gatatcattt tagggcttga 720
acctggaagt ttgcctccag ggtcatctga acctggattc aggttcagat ccagggccat 780
ctgaacctgg atcgtgtgtg tgggaaagac ccaggaccca cacacaatgt cakcagctgt 840
gtgtaattgt gtgctctgtg tgtggctgtg aatctgtgtg tgtgatttgc ctgttgattg 900
tctttggcat ggctgtgggt ccacgggcgg tgagggttcag gagtctcga 949

<210> 90
 <211> 1171
 <212> DNA
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (291)
 <223> n equals a,t,g, or c

<400> 90
 gaattcggca cgagcctctc cagtgccttat gtaaagaaat gaaagtattc aggggaaagct 60
 gtgctttgtt ggaggaccgc gttgtggatt tggccacett gtcacttgaa gtcgtgttag 120
 ggggtgcttca gcaggatgtg gccggatgcc ttctcatgat atgctgcaca gmaaactggt 180
 gctcttttstg gaagcctttgt ggtactacgg tgggggggct ttcctttgct gtgcccggctc 240
 tgtacctact gactgttatt ttgggggggct ggaccaaaga agacttgtea ntgataaatg 300
 tactgagaag agcacaggac tcttttaagt ctcaagggtgc tctgggctta gttcttctga 360
 gcaggggaaac cagaggcttg cgtctgtttt tctttktgta aaatggaaaa atacctgcca 420
 ttgccactta actaagtcac tgaagagatc atgtgcatgg aagatgtaaa acagtatgcc 480
 tctttataag taagggtggca ttattacttg agctgggtgga aggcagcacg ttccccacaa 540
 ttggtctcaa aagccccgga tgcctgctga gttgccattt agtttattac cttagcaaag 600
 cagagttggg ggtgcgattg tcgatagtag gctttgggag aaatgatkgc tatatttcgt 660
 aataaatgat gtccttgaga aactcataag ttgcaatgta atcctgtctt aattgtgttg 720
 ggcacractc ccactgcaat accttaaata actgaaaaca ttgccccttg aaagccccc 780
 tcgacttgga caataaaaaac agttgcatgt tttgctctag agatattttc tgcctttcc 840
 atcattccac tgcctgggta ttcttaggga gaataacaga taggatactg gggcttcacc 900
 actatttgat caggtatcag ttgaaatag agaattctctg ccttatgaag atagtaattc 960
 ctgtagttag catgaaaaca aattgccagt ttgattttct aggacagctc aagcagaatt 1020
 tgtaccacta ggctgtaagt tttaagtatc taattttctg atttgaaagt gtatgattta 1080
 aaaattggaa aaagtttttg ttataagctt caaaaggatt tactataatt acaatacgt 1140
 aaattacaaa aaaaaaaaaa aaaaactcga g 1171

<210> 91
 <211> 1151
 <212> DNA
 <213> Homo sapiens

<400> 91
 ggcacgagtg tcaatgaaag tgtttctaat gcaactgcga ttgactccca gatagctaga 60
 agtttgcaca tcccactcac ccaggatata gctggtgacc caagctatga aattagcaaa 120
 cagagactca gtattgtcat tggcgtgggt gctggcatta tgacggtgat tctaatactc 180
 ttaattgtag tgatggcaag gtactgcagg tccaaaaata aaaatggcta tgaagccggc 240
 aaaaaagatc acgaagactt ttttacacc ccaacagcatg acaaactctaa aaagcctaaa 300
 aaggacaaga aaaacaaaaa atctaagcag cctctctaca gcagcattgt cactgtggag 360
 gcttctaagc caaatggaca gaggtatgat agtgtcaatg agaagctgtc agacagccca 420
 agcatggggc gatacaggtc cgttaatggg gggcccggca gtcctgacct ggcaaggcat 480
 taaaaatcta gttccccatt gcctactgtt cagcttcac cccagtcacc aactgcagga 540
 aaaaaacacc aggcctgaca agatctacca ccagccaaca catttggtggg agcaggagac 600
 aacatttcaa ttggatcaga tcaactgctct gagtacagct gtcaaacc aa taacaagtag 660
 agcaaacaga tgcgtctaca tccatacatt actgtgtttg gctgaattcc actctaatat 720
 gatgctccat tatgcaccat actgtgatga cctttctact ccgaaacctg ctggagccgtg 780
 cccttggcgg tgggggtgta gccaatcact gcttgttcca cttgttgtac attttatttt 840
 tgagtctttt tctttctcat atacagaaaa atagtatgaa aataaaaata atgtatgaaa 900
 cagtattaat gcagaaatgt gctactaatg gatgtctgag tcaccagaaa ttccattctt 960
 aaagaggcgg ttagcaccta ttagacgtaa cagtgtatgtc ttttaaaaaa tccaaaagca 1020

tattgcaaca ataagctga gactttgtgt gaacaaaggg aaattctgcc tcttatgtct 1080
ttgtcttttaa tacattaaat actgattttg aataaaaaatc taaattgatc aataaaaaaa 1140
aaaaaaaaa a 1151

<210> 92
<211> 714
<212> DNA
<213> Homo sapiens

<400> 92
ggcacgagta atgcttctgt ttctcccact atatgcatat gtatgtgtgg gtacgtgcac 60
atttggtttt ttatttggtt gtgtgtctat ctgaaagttc tgcagggcag cgcttgcctt 120
tggattgctg ctgcagtggg gatgagaagg atgaggaaag tgcaggaaaa aggggagggtg 180
ttcaggaaca tggcggccac ctggggccctt cgttctggca taaaaagcct gaattctctt 240
gttagctctg ccttttttac tattttcatg accttgggct cttcttggaa cctcattgtc 300
tcactttcct cattggtaaa ttggaccggg cttttttctt tctacttctc aagaaactga 360
tgaggattaa tgagatagaa tctggagccc gttttgtgtt aaaaagagtt aagggatgct 420
agaagacgga gttaatgtca tagagaaggg gaacacacat tgcttaccgt gtgatgtgat 480
agagtctcag ggagcacttc tctttcaact gttaactgtt aactagttag gcagggtggca 540
gcctcatttc tatttgtgtc tgaagtggat gacatgttag tgcaggatga taggaagtca 600
aaccaaatgc agggactggg ggaatgacga gtcaagattc atgggggaac atctagcctt 660
ctgcattgct acctgaaaga aacttagcta tttaaaaaaa aaaaaaaaaa aaaa 714

<210> 93
<211> 810
<212> DNA
<213> Homo sapiens

<400> 93
ggcacgagtc ctgcctcatt tttctgtggg cctcatttgg tatgcaagga aataagccaa 60
acagcctgaa agtccagtag aagtgcagac cagacatccc agtcctccct gtaggggtttt 120
ctcagaactg ttcttttaag gtctcaggct gctggaaggg agggctgata gcagaaaaag 180
tggggacact gggaaactcca aagggaagac gcgcattggc tgaaaccgag ttctttcgtc 240
ttctggagcc tgggtctcct atgtggaggg tcatgctggc atggctggca atgggttaatt 300
caccgatggc catggagtcc caagttggcc atattattgc ggtaaaagat acattaacct 360
agatgacctt gccggggggc agaatagagc ccgtgaggaa ggagagcaag gcaggatcgg 420
ccgggaagcg agagggattt tggtgaggag caaggtcttc cacaggaact gcgacttggg 480
aagtattcac caagggctgt gccatgcgaa accctcttta aagggaaccgc atcgtagcc 540
taacgggcat ttctttttta atgtaatggt tcagagctat tgtctaccac gcctcgcgtg 600
cacacgcaca cacacgcaag ttccctcagt cagccgagaa tcttgccatc tcttttagat 660
aacaaaagct cttaggcctt atgctttggg taggatttgt cttccatgga cagggtattca 720
gttggaaca agtatatagt cactgcctct atggtatgga gatactccga ttagtcctt 780
ctgcctcttg gggaaaaaaaa aaaaaaaaaa 810

<210> 94
<211> 1176
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (569)
<223> n equals a,t,g, or c

<400> 94

ggcagcagtg	agcttgagga	tgcatctat	aaagccagcc	aatattaatt	actcttcaa	60
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tccttcttcc	aggaattgtt	agcataaata	ctgacagttc	cagacagtat	ggaaggatcc	180
cagtagatag	ggaaaagata	cccactcgaa	ggccaagcc	tagtgggata	cctttcctgg	240
gcacatgggt	ccaagagatg	acttaaatat	ctacaaccac	ttgtcagctc	agtttttttg	300
gggactactc	cagaggtgtt	ccttcacaga	ggcagtggtg	gaaaaagtaa	ggtagaaaaa	360
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ttggatgttt	tttgtttatg	ccttatgtat	tgacgttact	gccaatgaat	tttgccttac	480
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gggcgggtgg	tattattaat	ccgggatgna	ggctggattt	attttttatt	ttaatttttt	600
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ttagcacatt	atttttgttt	taagatgtca	gcacctgatg	tattatttta	gtgtctgttt	840
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gcttacaaga	acatttcttt	atcaagttta	tctggatttt	ctgggtcaaa	agtataagtg	960
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attttaaaaa	cacttagtga	gctaaaacgc	agactcaaac	caaactaatg	aaagctattt	1080
aagagaagtc	agttgaagta	gtttccagaa	tttatctcat	tgttttttca	actctttgtt	1140
aacaccataa	acgtgaatta	aaaaaaaaaa	aaaaaa			1176

<210> 95

<211> 1028

<212> DNA

<213> Homo sapiens

<400> 95

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cgggctgtga	ggttcatacc	gtgctgatag	cactcgtggt	gtctgtgaaa	tgtgggtaag	120
acattcaaac	ctggttttga	tactggaaac	tcttctttta	aaactgtgac	catgatttca	180
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gtggaccact	catctgcagg	cctctcctgc	atggggaggg	taggcaggga	gcagcatgtc	360
tgcaggggtg	aacctttgct	cttctgtcag	gcgaggccca	ggctgcacca	gccacctgcc	420
acatggtgac	agtgccacgg	gccttgcgta	tggccctctg	aacctgtctc	tggcgggcac	480
acctggctgc	tgcaggccaa	ggccgctgtt	cagtgaagag	tcccatgttt	agtatggact	540
aaagtcccat	gtttagccay	tgcccagtc	tcccgtgacc	ccagaaacca	ggtcactgga	600
ccacagtgcc	agatcctcat	cacgcgggtg	agcacctaga	agtgagaaca	ctgtattcct	660
acaatgtaca	cttgatatt	tctccttatt	tagttttctag	tgaacaaat	caagtaagga	720
actatcttta	gtttagatgg	aattatttgt	ttttaattgt	tgccgtattc	atctatatag	780
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aaagtcatgc	actttattta	taggctctat	gttttggctt	ctgcagtact	tttattatct	900
atacataatt	tggccaaaaa	taagaaattg	gaaagaatga	aatgtttagt	ttatagtaga	960
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gcacgtag						1028

<210> 96

<211> 747

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (605)

<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (642)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (645)
<223> n equals a,t,g, or c

<400> 96
tcgacccacg cgtccgccc aaggaatcct gagtatgtat gcacttttaa agaaccacaga 60
atcatctaaa tattgtcaca tggctcttgc aagtgatgat aatagtgatg cttataataa 120
tgaggattag ctgcactcat cagcctgtag aaagtaaaaa gtttcctttt cgaaattttcc 180
tttcttggtta agaataaatc ataagtgtta gaaataatag tttcttttaa agactaaactt 240
ccttcaagcc ttctctgtct tgtgctaata actcttcgtt aagccctatc ctatgtagct 300
gttagatata agggaataag tatattctat gtctgtact tttagccaaga tatttgtgct 360
ggacatgtct acaggcacgt tccagctggc agcctatgcc ccttccttat ttggaaatat 420
tattactttt ctaagtcttt ttgcaagcaa cttctctttt tcttttggtt tctgttgctt 480
ttccctatat aggaaagtgt taagtattta gccagtcggg tttaatttaa attgtgaggt 540
ccagctccag ccaatggaga caggacacaa gctgcataag ggataaaaac tgcttccctc 600
cttntttcgg gtgtgtgtgt accattgttt catctgtgag gngcncctt tctgccagaa 660
agtaaaattg ccttgtctgaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720
aaaaaaaaa aaaaaaaaaa aaaaaaa 747

<210> 97
<211> 628
<212> DNA
<213> Homo sapiens

<400> 97
cggcaccgagt atatatatat tttttaatat atatataaaa agacttttag atagaattct 60
catattctga tgacctatca cgttggttgt gcatttttaa tctgggtgct aaagaaacag 120
tttatactag ctctgcagac tatttcaaca tcaactcagga gcaaacaaat tcttatgggtt 180
ttaagcagta ctattattgc agattcaacc ttttattatt aatactttaa aacagggaag 240
aggttataag atgtggagct cattggagag taaaatttaa ccaacaaaaa ggatatgaca 300
aagtacaarg gaaaacaaaa ccaaaaaact tcatgtatcc caaaaaatta attttgccga 360
taaagtcttt aaaagtgggc aaaaaaggag gtttctcagt agaattatc gcaactaaag 420
gcaaatggaa aactctcaca tagcatttaa taagggttta catgcaatat atcccactat 480
cccaagaaat atctgcagtt caaagctgct ttttaattaa atgcttccta gtgtttgctg 540
tttataaatc ctaaatatta aaggggtgagt tctttaataa tactattcta ataagtacta 600
agacttttct aaaaaaaaaa aaaaaaa 628

<210> 98
<211> 904
<212> DNA
<213> Homo sapiens

<400> 98
ggcaccgagat cgtcttgtga caagacttgc tgagaagcac cttaaaattc actgtgagcc 60
acattttgtc ttttactgtc tcatcggata gggtagatca atgtccttta ctgtagcaga 120
gactctctca tgggcaggac catcatggaa agttctgact acatcaagaa aggcgccaat 180
gtctcacctg tgcctggggc caggcagcag gctgtgatgc cgggtgcctct ctgggttggt 240
ctgtgggtct gcttcctgtt atatgtagcc tcacgaagga cctttggatt agccaattac 300
atgcccctac cctgagcttc ttccccagct ctttgacttc ctggacattg gtgaatatcc 360
tgaataagca aaagggataa aattcataga aatatggtgg caaaaatata caacttcagc 420

ccagttctttt	gggtccatgt	tggtaaggag	tccagttggc	aagacaagct	gtccaaggaa	480
gtgcctcaga	agtctgggtc	aaagaggagg	gccagatctg	ttctgtgaga	ccctatgtga	540
ttgttatatt	tttaaataat	atataattaa	gcaggacaaa	ttaaatactc	catggctttg	600
gggaaattgt	tgctttaaag	tcctggaatg	gggctgggca	cggtggctca	tgcctattaa	660
tcccagcact	ttgggaagcc	aaagtgggtg	gatcacctga	ggtcaggagt	tcaagaccag	720
cctggccaac	atggcaaaac	cctgtccatg	gtggtgtgcg	aggctgaggc	aagaaaatcg	780
cttgaacccg	agaggcagag	gttgcagtga	cctgagattg	cgccactgca	ctccaacctg	840
ggtgacagaa	tgagactccg	tctcaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	900
aaaa						904

<210> 99

<211> 576

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (12)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (521)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (535)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (572)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (576)

<223> n equals a,t,g, or c

<400> 99

aaattccccg	gntcgaccca	cgcgctccggg	caacattccg	ttacatagag	aaatctatgt	60
aataagctgt	gtcataacac	ccatcagttg	tatttatgat	ctttattaat	gtattttgtt	120
tttaagatct	tttttcagag	cctctgtgtg	ctgggttact	gtatacttcc	cttgacagta	180
gcaatgctga	tttgccggct	ggtacttttg	gctgatccag	gacctgtaaa	cttcattggt	240
cggttttttg	tggtgattgt	gatgtttgcc	tggtctatag	ttggtaagta	tgtacttatt	300
tccacaataa	cagaacagac	aaaaacatga	tttaatgatg	aagaccagat	gaggagcagt	360
ataagtccaa	agttagatgt	gagtgatatg	attcttgata	gtattatcca	tagaaccctc	420
ttccctgagt	aggcaatgat	ggggcttata	tgagttggat	atctggactt	ataagatgtg	480
gagagtcaca	tcktttttct	ttcttttaaaa	aaaaaaaaaa	nggcggccgc	tctanaggat	540
ccctcgaggg	cccaagctta	cgcggtggcat	gngacn			576

<210> 100

<211> 713

<212> DNA

<213> Homo sapiens

<400> 100

ggaagaggtg	caagcaaagg	ttttacgtat	gatcaatgtt	tacttttagcg	gcoctgggggt	60
gctaacgcct	ttggatgacc	aaggctcacc	ctgccctccg	gcaccttttg	ctgctcttca	120
cccttgccct	cacctgctg	gctcaggggt	gctgtgctgt	tgccccctca	ggctgtgccc	180
accttgagg	atthttgttca	ctgggcccact	cctgctgacc	cttcaccatc	tgtctgtga	240
aacctctccg	agtgggtatag	gagttggaaa	catagtccct	ggggccagac	ctttgggtgt	300
aaatccagtc	tttctatatt	ctagctgtga	ccttgggcaa	gttctgagc	cacttttggt	360
gaccatttcc	tctgaaaat	gaaactaatg	atagtgccta	cttcacaggt	aaataggagt	420
atgaaatgaa	ttcacatata	taaagcttct	agagcatctc	ttctcagtag	ccaacatcct	480
gattactaat	ttgcgggggg	tggcactctc	tctctttttt	ctctgctctt	tgcagggtgt	540
gccaccacta	acaataaaact	atagggagga	gaaaccaggt	caattccctg	aaaagtctcc	600
agtgtgacca	gaagtacaga	taatattgtt	ccattgtatt	aaagtcattc	tagggagtct	660
tagaagatta	gatgcatgtt	ggttcctaca	gaggaaaaaa	aaaaaaaaaa	aaa	713

<210> 101

<211> 649

<212> DNA

<213> Homo sapiens

<400> 101

ggcacagggga	agtgtcaagg	gggcgctccc	ccatctccgc	cgtattacc	actgaacccg	60
gacccccctac	ccaggtccag	ggccagccgc	catgacgaac	gtgtactcct	tggatgggat	120
tctgggtgttt	ggtttgcctt	ttgtttgcac	ctgtgcctac	ttcaagaaag	tacctcgtct	180
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gattggaacc	aggctgcatg	ctgctgtggc	aattgcttgt	gttgaatgg	ccttttacgt	300
cctgtttata	aaatgaattc	caaagcacc	aagtcacaa	ctgccaacca	aggggacggg	360
gatgaagaac	ctgttggaga	cctgaaccca	gtgtaggaga	gttcagctga	aatcatcggt	420
ccccaggatg	acaccacagc	atctgcccct	gctatatgtg	gggaaaactc	atggtcacga	480
acattatttta	tgtttcagg	gactacagaa	agccagcttc	ctttgatcta	tgtgtaaact	540
agtccttggc	agagtgcata	taatgtccgg	ataaattaca	cccctcggtg	ataagattac	600
atacctcctt	cataaaaacc	tgtaaaaaaa	aaaaaaaaaa	aaaaaaaaaa		649

<210> 102

<211> 697

<212> DNA

<213> Homo sapiens

<400> 102

gatttagggga	gggggctgtg	atgtaaaacg	tctcccctgc	caaaggagg	gcaaagtgt	60
gtgtcagttc	ctgtttcttc	ccatttccctg	gcacactctg	ccctctgtc	cgggggacac	120
gcgcattgtgt	ttgccaggga	tggggccacc	gggttgatgc	caacgtccg	ggtgctgtc	180
ttgtctgtgt	ggcttctcag	atggtggagg	gtgctgggag	ctggcagggt	ccttcagac	240
agtctcagcc	tctcccgc	gcccccaaca	ggctgtcaaa	caaaaccgga	gagggggtgg	300
gggagccagc	ctcccagcgt	gctgtkcccg	caggcacccg	tgtgacatcc	gcacgtccag	360
ctccgtgacc	tgtgtgtgtg	tgtgtgtgca	caagtgagt	agagatttgc	aacgccacc	420
cctcgacttt	gaaatctgag	caaaacaaga	aactgggggtc	ttctctctcc	ccgaacctct	480
ccccagctag	tcttccctct	gttcttccctg	cctccagccg	cccgcgccag	atthttgaaat	540
ctcggagaca	aaactagtag	tgtgaagataa	atthtttttgt	actgtattta	ttgtgtataa	600
cgattthttt	aaaggagaat	tctgtacatt	tagaactctt	gtaaattaaa	aaccgatcct	660
ttthtttaaaa	ctgtaaaaaa	aaaaaaaaaa	actcgag			697

<210> 103

<211> 1288

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (462)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (813)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (825)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (834)

<223> n equals a,t,g, or c

<400> 103

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cagagctact	ttcagcattc	tgttttccgt	agtttgcttg	ctcttccctg	gttccatagt	180
gaactgtttt	ttaaattgat	tcttcaagcc	actgaccctt	aacttttcca	ccgcactctc	240
agcatggaga	aaagagtcac	cagcctggaa	tcccttgggt	ctcctaccac	caacagatga	300
atatcccaca	tgagcatcca	ccttcggccc	ctttccctagc	tcagtgggct	tccttccctat	360
tagtgtctgg	ttttctattc	cattcagttc	ctacccttcc	tgcctgctca	gagtcctcac	420
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gttaggttgc	ttaagatatg	gcctccagat	ccaaccatgt	tgtcgcaagg	acatgatctc	960
tgtctttttta	tggtctacata	ggattccatt	gtctatacgt	accacctttt	aaaatccagt	1020
ctatcattga	tgggcatttta	ggttaattcc	atgtctttgc	tatagtgaat	agtgtctcag	1080
tgaacatact	catgcacgtg	tctttatgtc	agaaacatat	ttaaaactaaa	gagcttctgc	1140
acagcaaaat	aagctataac	agagtaaaca	gacaacctac	agaatgggaa	aaaatatttg	1200
caaactatgt	atccaacaaa	gatctaatat	ccagacgcta	taagggaactt	aaacaaattt	1260
acaagcaaaa	aaaaaaaaaa	gggcggcc				1288

<210> 104

<211> 1027

<212> DNA

<213> Homo sapiens

<400> 104

gtccgcccac	gcgtccgtac	aatgtatggt	gtgtggttgt	gtgtataggt	tttgataaat	60
tttaactttt	ttaaatagat	ttatgtatgg	tagtaaatga	tagactagta	tctacatgta	120
ttttatgtac	tcttcacata	cttttatttt	ttttgatatt	tctagtctat	gaggttcate	180
tggtttttca	aattgttgca	aatctccaaa	aaattttcca	atacatttat	tgaaaaaaaa	240
tccatgtata	agtggaccca	cacagttcaa	acceaggttg	ttcaaggatt	gactatttgt	300

ctatctaaac	atacctaaac	atagraaaagg	tacagtaaaa	atacagctatt	ataatctttat	360
gggatcacca	ttgtctatgc	aggctgacat	tgaaatgtca	ttatgtacag	catgactgta	420
tagtgtttcc	gagttctgtg	aggctctcta	gcaaactaat	ggagctcaag	aaggggttat	480
gggaacccta	acttatagct	agttgggttag	gaccttggg	caccatctgg	ggcttctgat	540
tgtcatctga	agtgggagcc	atcttgtggc	actgagcytt	caacctatgg	tatctgatgc	600
tatctccggg	agtgttaagaa	gtgaattgaa	ttagaggaca	cccagctggg	gtctgctgca	660
aaattgctta	tttgcttaaat	gcgtggggaa	ccccctcca	cacacatctg	gagtcagaaa	720
gggtgtttgtg	agattaaagt	gggagaaact	gaatttgttt	attcctatat	tcagaatggg	780
gtccttgara	acatcatagt	ggtaagcata	gatgttctaa	agtcagactg	cctgggttca	840
tctctctgct	ccaccacttc	gagagttact	ttagctcact	gtgcttcagt	ttcctattaa	900
attgggataa	taataccatc	tcatagagta	acttaagaat	taaatcagtt	aatatacata	960
aagcacttgg	aagtgtttga	agcattaata	aacactcaat	agctaaaaaa	aaaaaaaaag	1020
ggcgggcc						1027

<210> 105

<211> 710

<212> DNA

<213> Homo sapiens

<400> 105

ggcacgagct	gggcctccag	gttcttcacc	tgtcacatga	tcattttaca	tattgtgggc	60
tgtttatttta	ccatcagcat	catagaagag	caaaaagaag	aaatactgtg	ctccactaaa	120
agccaggctg	agaaaacagt	tactcacatt	gagcagtgag	tgaccactag	gtgggcattt	180
gttcatagct	gcatggagaa	caagtgcaca	tatacatctt	tctgctgatg	cagcctctaa	240
atattgaaatg	catcagtttt	ttaaactgca	ttgagcaata	ttccgtgggt	gtgatccata	300
atagcgtaac	tatttacgcc	tgtgacagag	aggaaaactg	tatggatatc	agatatcttt	360
aagagctttt	taatctttta	tcaagttagt	acttcttaag	gatgattaag	gccaggcagt	420
ggctcacacc	tgtaatccca	gcattttggg	aggccaagat	gggtggatcc	cttaaggtea	480
agagttcaag	gccatcctgg	ccaacatggg	gaaaccccat	ctctactaaa	aatacaaaaa	540
ttagctgggg	tgtgggtggc	ggcgccctgt	acccagctca	ctcaagaggg	tgagacaaga	600
gaatcgcttg	aagccaggag	ttggagattg	cagtgaagca	agatcatgcc	acttcactcc	660
agcctggaca	gcagagtggg	acttcttctt	aaaaaaaaaa	aaaaaaaaaa		710

<210> 106

<211> 530

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (16)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (22)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (45)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (47)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (54)

<223> n equals a,t,g, or c

<400> 106

ttggcccccc	taggggncctt	tngccaaaaa	aggctatctt	agggngnccc	cctntaggaa	60
gggtaccccc	cttcagggtac	cggccccgga	attccccggg	tgcacccccac	gsgtccgccc	120
cacgsgtccg	cttttggttg	gagaacagct	ggctaaggat	gactctaagt	gtactgtttg	180
catttccaat	ttggttaaag	tatttgaatt	taaatatttt	ctttttagct	ttgaaaaatat	240
tttgggtgat	actttcattt	tgcacatcat	gcacatcatg	gtattcaggg	gctagagtga	300
tttttttcca	gattatctaa	agttggatgc	ccacactatg	aaagaaatat	ttgtttttatt	360
tgccttatag	atatgctcaa	ggttactggg	cttgctacta	tttgtaactc	cttgaccatg	420
gaattatact	tgtttatctt	gttgctgcaa	tgagaaataa	atgaatgtat	gtatttttgg	480
gcagacacct	gaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	gggcggccgc		530

<210> 107

<211> 392

<212> DNA

<213> Homo sapiens

<400> 107

tgcacccacg	cgcccgccca	cgcgtccgga	gggaacttaa	atgatattcc	ccttttcctt	60
ttccctaata	accttcctgc	cagattttca	agtaggcaat	gataacagca	ggtgagatat	120
taggaactgt	gactacgaat	atgtagatgg	agatgtgcag	aaggatccag	agacttagag	180
caatgcttca	catgcttttg	gtaagcatgc	tccctactgt	gggtaaacca	aacatgtacc	240
aaccccccca	gaattatgat	attctactgc	agtaaccagc	ctcttctttt	aacatcagat	300
agctaaagga	cgttatcctc	aaagtcatgg	aaaagcagga	agtttttcat	gacaaatcag	360
tttgccatag	tacagttaaa	aaaaaaaaaa	aa			392

<210> 108

<211> 991

<212> DNA

<213> Homo sapiens

<400> 108

ggcacgagga	attttgtcac	gtgagctgtt	gggttactga	gtgagtgaag	ttcactgtct	60
gcaattgagc	ccttttgagg	attcttaaaa	cttcagcctt	tttcagtctt	tccatctcat	120
tccccttaaa	gaaacacatt	tggactttgt	ctggctctct	ggtaaaccct	gtgacctgca	180
ttactagggc	acagtgcac	agaaaagaaa	gtgtgtgttt	ggtaaatatt	tattgagcac	240
ctgcagtctt	atgttttagc	gtatgcattg	tgcctgtctt	tggaaagcaa	agcaaaccag	300
ttcatcagca	ggttttcttt	gcctgcattg	scgtgtccca	gccttgcagt	tgacacgaga	360
gaaatataaa	acatggccct	ggccttcctt	cattttaaca	ttcttytttc	ccaagcactt	420
actctgtgca	aggagctgga	gaagccaaa	ctggagaaaa	acaaaggagg	gcctgccttc	480
gagaagttag	tgggtctaat	ttgtggttct	caaactcagg	cgtgcgtttg	aatcgtctgg	540
gggccttgcc	agaccacaga	acctatcccc	tgagttttct	aatcaatggg	tctgaggttg	600
ggctcgctga	gaattttgat	ctttataaat	tccagataat	ggtcttgccg	ctgggttaggc	660
acctatgggt	aagaaccact	ggtctggccg	ggcgcggtgg	ctcacgcctg	taatcccagc	720
acttcggggg	gccgagacgg	gcggatcacg	aggtcaggag	atcgagacca	tcttggttaa	780
cacgggtgaa	ccccgtctct	actaaaaata	caaaaattag	ccgggcgtgg	tggcgcgcg	840
ctgttagtcc	agctacacgg	gaggctgagg	caggagaaat	gcatgaacct	gggagcgga	900
gcttgacagt	agtcgagatc	gcgcactgc	actccagcct	gggcgacaga	gcgaaatccg	960
tctcaaaaaa	aaaaaaaaaa	aaaactcgta	g			991

<210> 109
<211> 912
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (896)
<223> n equals a,t,g, or c

<400> 109
gggtcgaccc acgogtccgc ctcaaggtgc ctactttgct gggtcccttt ccagcagctc 60
ccccacctcc cttagecccc cctcctctgg cagcctctcc tgccctctgt gagctccctc 120
ccacgtgttc caccctctta ccttctgtgt gtttacatcc aacctgctg agaatttcct 180
ctggggagga atctatctct gtcattgtct agtgccctgg agggagagaa ctttctgggg 240
gtaggggtgc ctcctctctga aacaggccag gtgagcatca tgcayaaggc ctccattctg 300
tccgctcaga ttctgggtgg ggccacaggc aaatctcttg acttatgggg agttggcttg 360
tggttccctcc cttggatagc ctccatggaa ccactatagg ctttcccaac agctgcctct 420
gaaatagctg ctgcttcgag atcctccctt tttaaagcac tttctaaagc cctcaggatg 480
gcgggagcra acagcactgg tatattctag gagtaagtgc aggaattcag cagtgagagc 540
atgtctggga ccacctggac tgcctccat ttaacctcaa atctctttgg gatactcgcc 600
ctccctggga accagagttc tggctctaac attgagcagc tatgcactag ttccagagaa 660
gccactaaca ggctgccatg tgtagatgta gggtcttaag agatcacagg ctgggtcctc 720
tgatcactgg atggatagct cagcctgggg catttagtgt tttccctggg gataaatccc 780
caagrcagct ggatttggag ctgggtggcaa gttgaaatta ttaaaaattg atttgtgtgg 840
gactgtcaaa aaaaaaaaaa aaaaaaaaaa aaaaaactcg aggggggggc cggtanccaa 900
ttcgccctat ag 912

<210> 110
<211> 875
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (66)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (872)
<223> n equals a,t,g, or c

<400> 110
ggcacagcgc gaggtctgggt cccggcccag gagaagggaag tcgctgaagg cagtggccat 60
gctggnctgt gaaatgggag gcggttgcag rgggtctatg gggcccggtc ctggatactc 120
ggcaggaagc cgtgtctgca gaggtctctc cctgcctcag gtggccccgt tcaaccccag 180
ccgtgccccat ctctgcccac cgcctgtcgg tgggggttta aattcgggtg ggctttcttg 240
ggtgcagctc agcaccctcc cttatgcaga ctgggagggg gtcgggcagt cccctcagcc 300
acgaggaccc tggatgggtt ctagtctact tgggacctg gggcctggct gcgtactgag 360
tgggtgcccc acagtcaagg ccaacggggg ctccccctgc tctgagatgt tgggagaaag 420
gcggcttctg gaaccttccg tgggacctgt aagtggctgt ccagaaaggc gggagggtgg 480
gcacggggca cggggggcag ctggggctgt cgttaagggt cacgcctccg tacagttgaa 540
tttcccttct cttatcatgt tttaccacc ttgtcccttt tttccccaat tgtgcttttg 600
catttttttc cttggcaaat gtaaaactcag cctttcatte atgacgtgtg aaatttcagt 660
ttctctggag tttgtcagac ggcgtgggaa ccacgcctga aactcaggta ataggaggaa 720

aaaaaaaaa	cttaaaaaa	ttttaaaaa	acataaaact	actctctacc	tttgctggsc	780
cagcctgtct	cgccttgccc	gcggcagggc	ggcctgtaac	aatttcagtt	ttcgcagaac	840
attcaggtat	taaaaggaaa	aaaaaaaaa	anggg			875

<210> 111
 <211> 459
 <212> DNA
 <213> Homo sapiens

<400> 111						
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ccttcagaca	caaagatgta	agctgaggga	aatgaattct	tggattcagg	gaaatgaatt	120
cttggtattct	gaacatgagg	gtcagattta	cattcctgtc	tcaattgttg	acgcttatcc	180
caaggactag	tcattctgca	acatctgttg	gaaattccca	gattgaactt	cccagggaga	240
aacatcatat	gacatattgg	gaaaatggct	gacaatgggt	ttccttagta	agttcattga	300
gaagaaaagt	gggcggatga	tttcccgagt	cttcactctt	tcagaagccc	ctaaaacaat	360
ctgacatgct	ctagttggag	cctgctttct	atcccatcag	tttgatttct	gaatgcctta	420
tgatcattag	cattcttcat	taaaaaaaaa	aaaaaaaaa			459

<210> 112
 <211> 609
 <212> DNA
 <213> Homo sapiens

<400> 112						
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gtgacaaaag	gtgtgccttc	tgttgccaca	tttgaccac	cacaggactc	actggactgg	120
acttctattt	atatggtatt	aagtaactga	tatatatata	tatatatakt	tttgattgac	180
accaaaaaat	taccttgcca	caaatgccag	acctgtgaag	gtcagaggcc	cgctgcttyt	240
cccaggaggg	agggaaacttt	ttggttgtct	gtggcaattc	ctctgtacag	attgtaactt	300
tttaaaaaat	tcccttcacc	cctgcacttg	aatatatgtt	catagtaatt	tgtaagatac	360
ttcttttctt	tatttttggt	gcaagacctt	tccgaacaca	ttcctgtata	aagtattttg	420
cactatttta	agaaacccat	atggatgaag	tcaggatgtg	caatatgatg	gcgtcacagt	480
gtcctcgtt	gtacctgtaa	tgtaactaat	cagtttaaat	gtactatttt	aaatatgtaa	540
aataaatttt	caccatgagc	atgttttaat	gaaaaaaaaa	aaaaaaaaaa	aaaaactcsa	600
ggggggggc						609

<210> 113
 <211> 1404
 <212> DNA
 <213> Homo sapiens

<400> 113						
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taagagtcce	atcttgccct	tctaaggga	agataggtaa	atgaaaagac	tgctaaatcc	120
aaggtcagac	agcatataga	aggctttata	aaagaacagg	aaaactcaga	acactaaata	180
agagagtgtc	ttcttgga	ctgcagttgg	cctcaatcat	cggatctgga	atattacttt	240
ttacgatttt	gsaagccgat	acacacctgt	aagtaataac	tgagggaagg	agagtatgat	300
tagtcttttt	acctttcagt	gtgtatcaat	gttaagtga	caagagcmaa	aggaaaacca	360
tatatattag	atattgcaac	atatataaaa	taacaacact	gggctggggc	tggtggytca	420
agcctgtawt	cccagcaytt	kgggagccga	ggcaggggga	tcacaagkct	aggagtttga	480
gaccagcctg	sccaacatag	tgaaaccccc	tttccactca	aaatacmaaa	aattagtcgg	540
gcgtgggtgat	gggcacctgt	aatcccagct	actcgggagg	ctgaggcatg	atgatcgctt	600
gaacctggga	ggcagaggtt	gtcgtgagcc	gagattttgc	cactgcacac	cagccccggga	660
aacagtgcga	gactccgtct	taacatgaaa	aacatgaaca	gccgctacta	tctgagggca	720

attttttgtc	ttttttttt	ggcatgtata	ttattttctac	aaatttttt	aaagggccagg	780
tgcggtggct	cacgcctgta	atctcagcac	tttgggaggc	cgaggtgggc	ggatcacgag	840
gtcaggagat	cgagaccatc	ctggccaaca	cagtgaacc	ctgtctccac	taaaaaacac	900
aaaaaattas	ccaggtgttt	ggtggcgggc	acctgcagtc	ccagctastc	aggagctctga	960
ggcaggagaa	tggcatgaac	cggggaggcg	gagcttgcag	tgagccaaga	tggcgccact	1020
gagctccagc	ctgggcaaca	gagcgagact	atgtctcaaa	atagtaataa	taataatttt	1080
aaaataaggg	ggaaaaaatc	actgataaac	caaaaacctc	aaccttaaga	aacgttcaca	1140
tctgtatagc	taatactctg	acgatgggga	tacaaaaaca	ccttcactca	gtggctctgc	1200
agatatcatt	tttttccag	tatttttttg	aaagaaccaa	tctttgtctt	tttttctcct	1260
tcttcaggga	actttatgaa	tccagaaaga	gccaacgttt	gaatgattac	tgcaatctca	1320
catctattaa	atcctgatac	ctgcaaccaa	gagatgagta	ggagatgtgg	atcctaagag	1380
gtgacctgta	acatactgcc	ccct				1404

<210> 114

<211> 853

<212> DNA

<213> Homo sapiens

<400> 114

gggtcgaccc	acgcgtccgg	gtgaattaac	acgtacccaa	tggccaagag	tagatttggg	60
tgctcagtgt	aaaattttca	ttttcaaaaa	cctggtgttc	tcagttacag	ctttatataa	120
gtatagtaat	aacttttagc	gagctgtaga	gagatagatt	tgcaaacttg	aagtgatatg	180
ggataaatct	ccatacgtgg	tagaatttta	tataaaatgg	catatttcaa	ggtatgtgtg	240
attatttggg	ttcagcaatt	ctgtgttgaa	gaaactagta	tcataaaaaa	tgttcgtatg	300
ctgacatcag	aattccagaa	ttcatatgcc	acccctgttt	ctgggctcct	tcctggtgct	360
gtggcttggg	ggggtgggtg	tgtgtacggg	tgggtgaggc	acgccatgca	ggtattgcag	420
aaggaaaccca	cgcaaccgtc	atccttttcta	cccccaagt	atgctgcctc	attctggggg	480
cctgaaaagta	ggcttcactt	aacatggtag	ggaagtttct	ggctgaaaaa	gcaaaaggct	540
tttatcactg	gagctctatc	tgagccccc	gtgcaaaagg	cagtgtgaac	tcaggggaca	600
gaatcactga	agctttttgt	aaagcacaac	atctgcctat	cacagtccaa	aggggacttc	660
aaaatcaaga	atgtctgtga	cggagaagat	ggaaacagag	cctggctgat	ggttgtagg	720
gaatctttct	tgtgtcagga	tgttatcagt	gaccgttttc	tttatttcat	gaagaaacat	780
ttttaatata	ttcacctccc	tgcataatatt	ctgtttactg	tgttattgtt	aaaaaaaaaa	840
aaaaaggg	gcc					853

<210> 115

<211> 845

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (845)

<223> n equals a,t,g, or c

<400> 115

aactagtggg	tcccccgggc	tgcagggaatt	cggcacgaat	ggatctgtgt	ggatgggtgtg	60
tgccctgggt	gtgtatgamt	gtrtgtctgc	acccactgca	gcagtaccca	agcctgccaa	120
gggcaccatt	tgcttgaaga	tgctttctgg	tgccaactgt	gcctgccaa	gacaggtgac	180
cagacagcat	tagacaggct	gtgacctgaa	caggcacggc	cagagccaag	ggggctgctg	240
cagctccttc	tccagctgtc	actgtctcca	gcccttctct	ccccctctcc	tggcacatcc	300
cccaaggcct	tcaggctgac	ccctggattt	cagaacaccc	ctcttcatca	gaacgtatcc	360
agcctggggt	ccatgcccac	caacagcaag	acaccagttc	ccctgcataa	acaggtgctg	420
aagtcaggag	gactcaggca	gacacactgt	acacatcacc	gcaagctctc	cttcagtcct	480
cccaacgact	wtaagtgagg	tgttaatatg	cctgttttac	agataaggta	actgaggatc	540
aagaagttaa	gtgatttgtt	caaggttgct	actgcagcag	ttttgtgggt	tcctctctaa	600

gatggagaga	agttacacca	ggacttagtg	cctgggaagc	aaagagggtga	acttactcgg	660
ccaggattgc	acagctgaca	gtgatgatac	cgatggctgt	gcttttagta	gctgcttaggt	720
accaggaact	gtgcttggcc	cttgacacat	ataatttcac	ggaatcctca	cagcagatta	780
aaaaaaaaaa	aagggtaccat	attgtcccca	ttttacagac	caccccttac	aagagtggga	840
tggtg						845

<210> 116
 <211> 760
 <212> DNA
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (13)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (300)
 <223> n equals a,t,g, or c

<220>
 <221> SITE
 <222> (425)
 <223> n equals a,t,g, or c

<400> 116						
cggacgcgtg	ggnccggacgc	gtggggaaaa	aataacaaaa	caaaaaacaa	gaaaaaaaaa	60
acacaaaacc	ccgtaaaatc	acaaagaaaa	tccaacacca	aaggcgcaga	agccggctgg	120
ccgtgggtgg	ggcagcgtag	gcgtasatcc	ctctcctctc	acttagcctg	ttgactcttg	180
ttattatcat	gatattcaca	aaacgcgcga	tgtttaaaaa	gtcatagatg	tcactctctc	240
tttgccccca	gggaggaaa	ccaccttctc	ttgccccttg	gcccctttgt	caggggccan	300
gggtctgccc	ggtgggggtg	ccaacaggcc	tgccccttct	ctcccctgca	tccagccatg	360
ggggcctctg	cgattgcccg	aagggttgc	ggctgggtcc	agggccagca	caggcccgag	420
gccgngetgc	ctgggtttat	ttttatttaa	ctttattttc	tgttttatga	gtgtgtgtcc	480
gcccaccccc	acccccttca	gtgttaagt	gggagccctg	ggggagtctc	tcctgcctcc	540
cagcctctcc	caagacctcc	cccctcgtca	ccagccatcc	ctctggacca	ggcagagggc	600
ggaccgggtg	ggcagggggc	tgagggtggc	tcggggccagc	ccaccagcca	atggaccctt	660
cctcagggcc	ccagtgtcgc	cctgcccctt	tttaaaacaa	aatgcccctg	tttgtaaacc	720
cttagacgct	tgagaataaa	ccccttccct	ttcttccaaa			760

<210> 117
 <211> 988
 <212> DNA
 <213> Homo sapiens

<400> 117						
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atcttgcaag	tctggctggc	tcctgtctcc	tcctttctgt	actggggggc	ctgtctggat	120
ggggcgccag	cgatgacccc	attgagaagg	tcattgaagg	gatcaaccga	gggctgagca	180
atgcagagag	agaggtgggc	aaggccctgg	atggcatcaa	cagtggaaac	acgcagtccg	240
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ctgctggaca	ggccgggaag	gaagcagaca	aagcgggtcc	aggggtccac	actgggggtc	480
accaggctgg	gaaggaagca	gagaaacttg	gccaaagggg	caaccatgct	gctgaccagg	540

ctggaaagga	aktgggagag	cttggcccaa	gtgcccacca	tgctgtggc	caggccggga	600
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tgaatggcaa	ccatcaaage	ggatcttcca	gccatcaagg	aggggccaca	accacgccgt	720
tagcctctgg	ggcctcggtc	aacacgcctt	tcatacaacct	tcccgccctg	tggaggagcg	780
tcgccaacat	catgccctaa	actggcatcc	ggccttgctg	ggagaataat	gtcgccgttg	840
tcacatcagc	tgacatgacc	tggagggggt	gggggtgggg	gacaggtttc	tgaaatccct	900
gaaggggggt	gtactgggat	ttgtgaataa	acttgataca	ctaaaaaaaa	aaaaaaaaaa	960
aaaaaaaaaa	aaaaaaagag	gagggggg				988

<210> 118

<211> 1947

<212> DNA

<213> Homo sapiens

<400> 118

gaattcggca	cgagttgtgg	tctattttaat	gccatgcttt	tcctgttttt	gtactgtttg	60
ttggttgttt	tgccatttaa	attaaccccc	aagcatagt	ctgaagtgt	gcttagcatt	120
cacaagtcca	agaaatattt	atgtaaagt	aaagctgcct	gcaagattca	agcctgggtat	180
agatgttgg	gagcacacaa	agaatatcta	gctatatata	aagctgttaa	aattattcaa	240
ggttgtctct	ataccaaact	agagagaaca	cggtttttga	atgtgagagc	atcagcaatt	300
atcattcaga	gaaaatggag	agctatactt	cctgcaaaga	tagctcatga	acacttctta	360
atgataaaaa	gacatcgagc	tgcttgtttg	atccaagcac	attatagagg	atataaagga	420
aggcaggtct	ttcttcggca	gaaatctgct	gctttgatca	tacaaaaata	tatacgagcc	480
agggaggcyg	gaaagcmtga	aaggataaaa	tatattgaat	ttaaaaatct	acagttatcc	540
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ttscgacttc	cttccacttc	actgcagctg	catattatca	cctgaatgct	gttagaattc	660
aaagagccta	taaactttac	ctggctgtga	agaatgctaa	caagcagggt	aattcagtc	720
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acctttctgc	cattcttgag	gccttaaaac	acctagagg	agttactaga	ttgtctccac	1140
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ttacagctca	taaacataaa	atgaataact	aargaatact	ttacaagcaa	aagaagaatt	1560
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ctgtgtwcaa	cttttaaaat	ctgactttgt	tttaaaaaaa	cataaactgt	tcattacatt	1860
cttcattttt	atcattttata	gttttatgca	tgtaataaac	taatattgtca	taagatgaaa	1920
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<210> 119

<211> 1448

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (1441)

<223> n equals a,t,g, or c

<400> 119

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agtgcgaagt	agcttctcgg	ctgccccg	ggccgggggtg	cggagccgac	atgcgcccgc	120
ttctcggcct	ccttctgggt	ttcgccggct	gcaccttcgc	cctgtacttg	ctgtcgacgc	180
gactgccccg	cgggcccaga	ctgggctcca	ccgaggaggc	tggaggcagg	tcgtctgtgt	240
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agcaccaggc	ctacgtgttc	ctgctcttct	gcggcgcccta	cctctaacaa	acaaggcttt	360
gccatccccg	gttccagttt	cctgaatgtt	ttagctgggtg	ccttggtttgg	gccatggctg	420
gggcttctgc	tgtgctgtgt	gttgacctcg	gtgggtgcca	catgctgcta	cctgctctcc	480
agtatttttg	gcaaacagtt	ggtgggtgtc	tacttttctg	ataaagtggc	cctgctgcag	540
agaaagggtg	aggagaacag	aaacagcttg	ttttttttct	tattgttttt	gagacttttc	600
cccatgacac	caaactgggt	cttgaacctc	tcggccccaa	ttctgaacat	tccccctgtg	660
cagttcttct	tctcagttct	tatcggtttg	atcccatata	atttcactctg	tgtgcagaca	720
gggtccatcc	tgtcaacctc	aacctctctg	gatgctcttt	tctcctggga	cactgtcttt	780
aagctgttgg	ccattgccat	ggtggcatta	attcctggaa	ccctcattaa	aaaatttagt	840
cagaaacatc	tgcaattgaa	tgaacaagt	actgctaate	atatacacag	tagaaaagac	900
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gatgtggctc	tctaaagccc	ctcattgttt	ttgattgctt	tctatagggtg	atgtggacac	1020
tgtgcatcaa	tgtgcagtgt	cttttcagaa	aggacactct	gctcttgaag	gtgtattaca	1080
tcaggttttc	aaaccagccc	tgggtgtagc	gacactgcaa	cagatgcctc	ctagaaaatg	1140
ctgtttgtgg	ccgggcgcgg	tggctcaegc	ctgtaatccc	agcactttgg	gaggccgagg	1200
ccggtgattc	acaagtcagg	agttcaagac	cagcctggcc	aagatggtga	aatcctgtct	1260
ctaataaaaa	tacaaaaatt	agccaggcgt	ggtggcaggc	acctgtaate	ccagctactc	1320
gggaggctga	ggcaggagaa	ttgcttgaac	caagggtggc	gagggtgcag	taagccaaga	1380
tcacaccact	gcactccagc	ctgggtgata	gagtgcagaca	ctgtcttgac	aaaaaaaaaa	1440
naaaaaaa						1448

<210> 120

<211> 496

<212> DNA

<213> Homo sapiens

<400> 120

tcgacccacg	cgteccgaact	gacacaatga	aactgtcagg	catgtttctg	ctcctctctc	60
tggctctttt	ctgcttttta	acagggtgtc	tcagtcaggg	aggacagggt	gactgtgggtg	120
agttccagga	caccaaggtc	tactgcactc	gggaatctaa	cccacactgt	ggctctgatg	180
gccagacata	tggcaataaa	tgtgccttct	gtaaggccat	agtgaagaat	ggtggaaaga	240
ttagccataa	gcatectgga	aaatgctgag	ttaaagccaa	tgtttcttgg	tgacttgcca	300
gcttttgcag	ccttcttttc	tcacttctgc	ttatactttt	gctggtggat	tcctttaatt	360
cataaagaca	tacctactct	gcctgggtct	tgaggagtct	aatgtatgtc	tatttctctt	420
gattcacttg	tcaataaagt	acattctgca	aaagcaaaaa	aaaaaaaaaa	aaaaaaaaaa	480
aaaaaaaaaa	aaaaaa					496

<210> 121

<211> 1174

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (1151)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (1160)

<223> n equals a,t,g, or c

<400> 121

gagaggttca	ggttgggtctt	gctggcatct	tcacctaaaa	taggggtctgg	cagacaggcc	60
catgcgtgc	atcctgcccc	cggcctgata	gatggcctgt	gaatggcttt	tttacatttt	120
aaaagtgggt	gaaaacaaat	taaaaatata	tttcatgaca	tgaaaatcat	gaaattcaca	180
tttcattatc	tgagaataaa	cttttatgga	tgcagccatg	cctgtctgtc	catgtcttat	240
ctgtgtctgc	tttgtgctac	ggctgcagag	tggagtggct	gggactgaga	cggaacgccc	300
tcctcacggg	gcccgcgtctc	tccaccagga	ccgcggggct	actctgagge	tctgcttctt	360
ccccagcggg	gttggcttcc	tgctattcct	cagtatcctg	ccttgggtcc	gagttgggtcc	420
ctctgscaag	agccgtttct	gtgtctcagt	ggatggcgca	ctgsccttct	tgttgggtacc	480
ttgactgata	gackgggtcc	tgttcackgc	yccgaagtca	tcccagaaaa	cctctyacag	540
ttgcatgggt	tgaacccagt	ccgcgtgtat	ttagagtttt	gtctcttgcc	ccttcaccca	600
gaacagcagc	accacaccac	ttcctgtccc	ctgtgactgc	ctcgcaactg	ggtctgttct	660
gtgagatgtc	gccaccctgt	ttgccatctg	ggaggatctc	actccttcaa	tttaactctgc	720
tctcttcctg	tattttttta	gtttctatgt	attttacttt	taggacattc	cagcctgggt	780
gacagagtga	cgggtctcaa	aaaaaaaaaa	aaaaaaaaag	cacaccagtg	tcttccattt	840
ctcttttaat	cataatcatg	ctttaaaaaa	taccctcgag	catatggagc	aaatttaaga	900
taattgttcc	ttttctgcta	attcattatt	actgtcatat	ctaggtctgt	ttctgtcgac	960
tgtggaccac	ttatgtgcga	tccgtggacc	acttgcgtgc	gatctgtcgg	ccgacgatga	1020
gcttgttcgg	atgtagctcc	atcgtaagtc	gaggagcatc	tgtgatttgt	cctctgctta	1080
tgggatatgt	ttttccgcta	ctragtctgt	gtagtaaatt	tttgactagg	aaaaaaaaaa	1140
aaaaaaaaact	nggggggggn	ccccgtaacc	catt			1174

<210> 122

<211> 1046

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (14)

<223> n equals a,t,g, or c

<400> 122

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ctcctagccg	ggtgacccag	gggatttatt	ttatgttggc	tttctctgaa	atgccaaagc	120
cacccgatta	ttcagagctg	agtgaactct	taacgcttgc	cgtgggaaca	ggaagatttt	180
cgggaccatt	gcacagagca	tggagaatga	tgaacttccg	tcagcggatg	ggatggattg	240
gagtgggatt	gtatctgtta	gccagtgcag	cagcatttta	ctatgttttt	gaaatcagtg	300
agacttacaa	caggctggcc	ttggaacaca	ttcaacagca	ccctgaggag	ccccttgaag	360
gaaccacatg	gacacactcc	ttgaaagctc	aattactctc	cctgcctttt	tgggtgtgga	420
cagttatttt	tctgggtacct	tacttacaga	tgttttttgt	cctatactct	tgtacaagag	480
ctgatcccaa	aacagtgggc	tactgtatca	tcctatatg	cctggcagtt	atttgcaatc	540
gccaccaggc	atttgtcaag	gcttctaate	agatcagcag	actacaactg	attgacacgt	600
aaaatcagtc	accgtttttt	ccctacgatt	acaaaactgc	cagtcctata	tggagtctga	660
tcacaagact	gcagtttctt	cacagatctc	aggaagttgt	cgtggggcag	aggcttttta	720
aaaacatgtg	attagggagc	tatctttatc	tgaataataa	cgaattttta	ggtaaaacct	780
gagatagagt	actacaaaat	catgtttgat	acttcagatt	ttggaagtta	aatcatgtct	840
gttattttgca	ttcttttagaa	acttgactaa	gtacctgaat	tcataattct	attctactgt	900
gcaacatagt	gatgattcag	aaatttttcc	tttggggaaa	aaaatgaata	tgaacatttc	960
catttgtgtta	agtgtaaaaa	ggtccagaca	tgatcataaa	atttaaattt	tatacaaawa	1020
aaaaaaaaaa	aaaaaaaaaac	tcgtag				1046

<210> 123
<211> 1160
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (325)
<223> n equals a,t,g, or c

<400> 123
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tatataatTT tagggatag acaatttaat ttcttgggtt tectgtctca tggacctcac 120
ttaaccagta gtatgtgggt gtttttttcta ccttttttct ccatcttatt taaaatttgt 180
tgggtgtattt cccttagtea aactaaagag aaacaatcat ctaatcttat gttttatttc 240
ttttgtatat gtacatatga gaggaggagg aagaaagaga tgaggagagg tgaaaagaaa 300
agatccctct gcctgattgg gcttngccag catatgatag cagtgcaggc ctggttccat 360
gagcagcatc agattcaaat ttcataaaaa aagagcccag aggaattgaa aaagagaaat 420
taaattcaac aaggagaggc attgtataca ttatgcattc acgatagggt atgattgaga 480
agaagctggg gctttgggaa aaacatatta ggtttctaat ttacctttt tgaatagttt 540
tctcccttct aaacaggggt ataataaggag aatgctgaat gcctctccat tgaatttgga 600
aactgccggg ccagcattag tgtgggtattg tctgccca ca tttttctaga tgcaagttta 660
agatcatgtt cagtgtgaac attgaggact ttagagatcg gagtccgaaa tgtgtcaaaag 720
ttaatgttaa tagatgctgt cctcattttg taactgtgac ttctaaatgt gaccttttag 780
ttcatatctc ataaatttgc catttaagaa gaaatacaga watgaaagtt tkaagtttta 840
ataaaaagtat atcttgctgg gtgcagtggt tcatgcctat aatcccagca ctttggggagg 900
ccaaggccgg cagatcactt gaggtcagga rttggaract agcctggcca acatggcaaa 960
accttgtctc tactaaagat acaaaaaaaaa taggtgggca tgggtgggtgca catccgtatt 1020
cctagctact tgggaaggctg aggcacaaga atcgcttgaa cccgggagac agagggtgca 1080
gtgagccgtg attgcaccag tgcactccaa cctgggtgac acagtgagac tgattcaaaa 1140
aaaaaaaaa aaaactcgag 1160

<210> 124
<211> 893
<212> DNA
<213> Homo sapiens

<400> 124
ggcagcagta agggataaag tgggcctgag cccagtaaat cctctgcagg aggcgtgaagt 60
ttctgaaaca agaagtggga gaggggttcag taggaagggt cacaagtgag gtcgacaaa 120
gagatccctg tgtttcccca tgagtgccac aagggaactgg ggtggaagggt ctgaggctgg 180
accagtcctg gatgcagtgg ccttttctgt gtgttcttcc tctgctccct caggctctgga 240
gggctgggag cctgctgcgt gctctggaac ttactcagt cttgttgagc cactttcttt 300
gggaaatgtg gaccatgtct cttaaagaac cagaattgct tctttccacc aagtcattaa 360
ctgtgtggag arggagagag cccctgtcag aaattggggg atgcagactg aacaatgaag 420
gaacatagca acaatgaagg aacataggga caatgacwcc accttgagtc cagtgggaatg 480
aggtgcggct gcattaaaga atgaggaamg ggacagagac aggtgtaaga gacgatggaa 540
caatcascca agaaagtcag ggggttggct gggcgcggtg gctcacacct gtaatcgccg 600
cactttggga ggtgtggcg ggcagatggc ttaagcccag gaggctcgaga ccagcctgaa 660
caacatggca aaaccccatc tctacgaaaa atgcaaaaat tagccaggca tgggtggcatg 720
cccagtcagt ctcagctact tgggaagctg aggtgggagg atggcttgag cctggcaggc 780
agaagttgca gtgagacaag attttttaaa aggcaggca tgggtggctaa tgctgtaat 840
ctcagcactt tgggaggcca aggtaggcgg atcacctgag gtcaggagct cga 893

<210> 125

<211> 1049
<212> DNA
<213> Homo sapiens

<400> 125
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tactcaggat ctacacgagg ttgttaattc atgttttgc ttaattgggtt actctgtttc 120
ctatttcctc ggtttccaat acttgtttgt agaaaacatc agttttgtgt gtatttgctc 180
ttggtcctaa agttaaggac actatacgca gagttaattg accttcattt gtgtgccagc 240
attctggggg gacataatgc ctgcaagtgt catattctta atatgtgagg gggttctata 300
tggagtagag ggtagttgc taaataacct ctgtaccctt tttctctgt ctcgatgtat 360
gcctctcatc tcctgtagat tgcctatttg tatgtattcc tagaaaaggc cttcgatagg 420
acgtctgtag ggktattccc ttctaaaggg aatgggtata cctctcgacc tatcaattcc 480
atttctataa atttatccca tagatatact cacaaatgtg taaaatgaag tatatttgaa 540
gtaaattatt aaagcmmtaa gagcaagcta aatgttcac agcaggaaat ggagtcaata 600
tatcttcgtc tgtctgtata atggaacaat atgtattatt atgaacagtt tttgagcaaa 660
taaaaaataag ctgaagttta aaaagttgag ttaaaaaagc aaggtgtaaa acagtatgcg 720
tagtatctgt gtacgtttgt agatactgta cacacatgtt agagggcaat ttggataaag 780
tattctgtgc tcaattaaca tattttccct ttgtcttctt ggctctactg gcttattacc 840
agtagcagtt actcgggagt taccagcta ctcaggaggc tgaggcagga gaatcgcttg 900
aaccaggag gtggagggtg cagtgaagtg agatcgcgcc tgggtgacag aacaagactc 960
cgtctcaaga aaaaaaaatg cttatgttct gtataaaatc ttcaawaaaa tgacgatacc 1020
agtaaaaaaa aaaaaaaaaa acctccgta 1049

<210> 126
<211> 1626
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (525)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (542)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (562)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (607)
<223> n equals a,t,g, or c

<400> 126
ccacgcgtcc gacgcggcgc acgcggcagt cctgatggcc cggcatgggt taccgctgct 60
gcccctgctg tcgctcctgg tcggcgcggt gctcaagcta ggaaatggac aggctactag 120
catgggtccaa ctgcagggtg ggagattcct gatgggaaca aattctccag acagcagaga 180
tggtgaaggg cctgtgcggg aggcgacagt gaaacccttt gccatcgaca tatttcctgt 240
caccaacaaa gatttcaggg attttgtcag ggagaaaaag tatcggacag aagctgagat 300
gtttgggatg agctttgtct ttgaggactt tgtctctgat gagctgagaa acaaagccac 360
ccagccaatg aagctctgtac tctggtggct tccagtggaa aaggcatttt ggaggcagcc 420

tgcaggctcct	ggctctggca	tccgagagag	actggagcac	ccagtgttac	actgtgagctg	480
gratgacgcc	cgtgcctaata	gtgcytkgsg	ggggraaacg	actgnccac	sggaggggaag	540
antggggagt	ttttccgccc	gnaggggggc	ttgaarggtc	caagttttacc	ccatggggggg	600
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cgggctctat	gacctcctgg	ggaacgtgtg	ggagtggaca	gcatacccg	accaggctgc	780
tgagcaggac	atgcgcgtcc	tccggggggc	atcctggatc	gacacagctg	atggctctgc	840
caatcaccgg	gccccgggca	ccaccaggat	gggcaacact	ccagattcag	cctcagacaa	900
cctcggtttc	cgtctgtctg	cagacgcagg	cgggccgcca	ggggagctgt	aagcagccgg	960
gtggtgacaa	ggagaaaagc	cttctaggg	caactgtcatt	ccctggccat	gttgcaaaaca	1020
gcgcaattcc	aagctcgaga	gcttcagcct	caggaaagaa	cttccccctc	cctgtctccc	1080
atccctctgt	ggcaggcgcc	tctcaccagg	gcaggagagg	actcagccct	ctgtgttttg	1140
gagaaggggc	ccaatgtgtg	ttgacgatgg	ctggggggcca	gggtgtttctg	ttagaggcca	1200
agtattattg	acacaggatt	gcaaacacac	aaacaattgg	aacagagcac	tctgaaaggc	1260
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ggaaggagaa	tgttttcttt	gtggcctcat	ctgtggtttc	gtgtccctct	gaaggaaact	1440
agtttccact	gtgtaacagg	cagacatgta	actatttaaa	gcacagttca	gtcctaaaag	1500
ggctctggag	aaccagatga	tgtactaggt	gaagcattgc	attgtgggaa	tcacaaagca	1560
aatagtactc	cagaaagacc	ctgtctcaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	1620
aaaaaa						1626

<210> 127

<211> 1177

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (484)

<223> n equals a,t,g, or c

<400> 127

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tgtttttattc	caaacgtcta	tgtgtctttg	ttcactgcag	ctcttqtccc	tttgacgtgc	120
ctcgtgggtgg	tgttcgtgg	gttcatccat	gcctaccagg	tgaagccaca	gtggaaagca	180
tatgatgatg	tcttcagagg	aaggacaaat	gctgcagaaa	ttccactgat	tttatatctc	240
tttgctctga	tttccgtgac	atggcttttg	ggaggactac	acatggccta	cagacacttc	300
tggatgttgg	ttctctttgt	cattttcaac	agtctgcagg	gactttatgt	tttcatgggt	360
tatttcattt	tacacaacca	aatgtgttgc	cctatgaagg	ccagttacac	tgtggaaatg	420
aatgggcatc	ctggacccag	cacagccttt	ttcacgcccc	ggagtgggaat	gcctcctgct	480
gganggggaaa	tcagcaagtc	caccacagaat	ctcaatcggt	ggtatggagg	aagggtgccac	540
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actccccaga	tcgtggagct	ccaggaggat	acccatcgcc	gacactcacc	tgtagcacct	840
cactaaccat	tcgactgagc	acactttcat	atgtgtatca	gcttttgtgc	taaaactctc	900
taagtacatc	cacctgtgta	ataggaacct	gtgaattgta	ctggatgatt	aatacaaacg	960
tgattgtttg	atgttgagta	taaattactg	attgtatgtg	acctgaaaat	tcaactgctat	1020
aagaaaggtg	gagtcagttt	gtatcagtta	ataggatgtt	catattccaa	ggatattagt	1080
tgttttttta	atcatcctat	atggctaaca	ttgtttaatg	aaagtaataa	tcaataaagc	1140
aatagaatct	aaaaaaaaaa	aaaaaaaaaa	aaaaaa			1177

<210> 128

<211> 1276

<212> DNA

<213> Homo sapiens

<400> 128

tgcacccacg	cgcccgccca	cgcgtccgct	taatatctgt	attcccagtt	gcctacggga	60
taaaagccca	aactccttag	cagagaatat	aaggccctag	ctcccacatt	atctcagcag	120
tcatcaccca	ctatgttcct	caagactgca	gccattaact	tttttagagt	ccctaaacat	180
gctgtttact	ttcatgcctc	tatcccggtg	tctgtggaat	gacttccctc	cttgcccttt	240
tcagtgttac	aaacccctat	tctttaagac	atagtacaaa	tggcatctcc	tgggtggcat	300
ctttcctgca	ggcctacagg	cctagtaagt	atcttctctc	tctgtgctcc	tgcatacctc	360
cattcctttg	ttatgacatc	tataacttta	ataagtacta	aaatctgtag	tcctacaaaa	420
ctcaggcata	gaactcattt	cctttatggy	tctataatgg	aactttaccc	aactctcacg	480
ttccccatga	ccacagatgt	ggaaaatttg	aatcttgaca	gttcaagggtg	aactcagtca	540
ttttcagagt	tttcatagtc	ccttcaagat	tgaactcag	ttcctgcaat	gtttgccctt	600
ttttctctct	tttgtctatg	ctgggagagg	cattgtgggg	agggttgtct	ggcttatggc	660
tcccatgtgc	ctctgcttga	taaaccacct	gagctttggt	cattagcagt	ctcctgtgcc	720
tttcacactc	aggtagtgtc	tgcacaggcc	actctatgtc	ttttccatgc	tgaagaaatt	780
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tggaagaaag	aactttcatt	tgtcttgaaa	tgagaaaaat	gttcttagaa	tattttgtat	1200
tactctctgc	tctgtcattt	atggtaaaca	aaataaaata	ataaaaaaaaa	aaaaaaaaaa	1260
aaaaaaaaagg	gcggcc					1276

<210> 129

<211> 1334

<212> DNA

<213> Homo sapiens

<400> 129

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ttccatgggt	tgttactgtg	ctgtaccact	tgggtgkctc	gattctgaac	ctgatgtgtg	120
tgttaattat	attttaagca	acacacacac	acacacacgc	ctcatgtaat	ggacttttat	180
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aaaaaaaaaa	aattttacca	atggagatgc	agtagagtcc	ataggctcta	aaaactaaaa	480
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tgagttcatg	gttcttttag	tcaccttaat	accagctatc	tttggtagaa	gctacagcat	900
tcagtttctc	tggaaactgt	atcacatttt	tgcattttta	aaattttaca	gtatcaaaaa	960
acaaaaatct	gcttatgaaa	caaaacatga	agcaggacat	atltggatto	tattttattta	1020
aaattaaatt	ccttgcaaaa	ttgaacttct	caactaaaac	gtgtccatgt	cagaatttta	1080
actgttagca	ggtagtttgt	ggcaaagatg	gctaaataat	gaagcaaatt	agaatctgtg	1140
tgtatactaa	tgagctgctt	tttttctgtt	gagactatca	ttatttgtct	tattacccaa	1200
gaggcaatta	cctgaatttg	gatgtctgaa	ttataactta	tgcaggaata	gttctgtaaa	1260
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aaaaaaaaact	cgag					1334

<210> 130
<211> 532
<212> DNA
<213> Homo sapiens

<400> 130
ggcagcagcc ttggggccatc tcctaaaatg atctttatca taatagctac agtaaaaaga 60
aagaaggaga ggtattaatg tgggtggaaa tcaggacagt ttctaatgc cgtggcttac 120
aattctgaga tttctccagg catcaggaca tgtgcgcgca caggacttgg ctctcttagg 180
agatacttca gtttgtatca gatgtggctg tggagggtgc tctttaagca ttgctaacta 240
tgagtgggtc cctctcagaa ggaaggactg taagaggtat gaaacttctg agaaaacgag 300
ctgtcttctc ttaccaagcg cctgcagccg tcaaaatgct gtaggcttta gtcgtctgcc 360
agttcccaag ctgagctgtc tcttcatgg ataggatttg tttgtttaga aacaacaaca 420
aagttcattc tgtttataac tcagagcatt tgtttttct gctgaggcta aaatacttgt 480
ttattcttct ctagaggaga aaagaaaaaa aaaaaaaaaa aaaaaaaaaa aa 532

<210> 131
<211> 685
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (491)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (661)
<223> n equals a,t,g, or c

<400> 131
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caatcttctg ttttttggtc agcagacaat cattttcttc gtaagcacct tttctctctc 120
actctgtcac tgccctgtgt ggtactgggt ataaatgtgg aaaaagaata gttatgactg 180
taacagattt ttatttttat ttcaaaatct tatatgaatt atgtatatct taatgatcgg 240
tcattttccc agtttgtaat atatgtgtag aaattgacct tatatgatct tgctttttct 300
cctctccctt tctcttctc tctctctcct ctctctgtct ttctccccgc tcaactgtct 360
cttttctttt tgggggtctc ctcccactcg gtgctcctgg tgcgacttg gcagtcaagg 420
agaggcatgg tggcctgggt taggaagagg gacctgtcg ctagcaaaag cggagagtga 480
gattgtagta ntcttatgca aaagctatct ccagtatttc ttagcagctt cagagggtatc 540
tctcactccc tgtagggcgc ttttactgtt atcttaaaact gcgtgtttat ctatatgtaa 600
aaactttcta aagcaaatac agtattctcc attttcttat caaaaaaaa aaaaaaaac 660
ncgagggggg gccgtaccat tcgcc 685

<210> 132
<211> 729
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (725)
<223> n equals a,t,g, or c

<400> 132

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tactaaaagc	accttcacga	gctgtgaaaa	atttaaatgca	tttatttaca	tatttagttt	120
taaatttttag	tatatgttta	gttgagggtat	agttttccaaa	caaagagccg	tgaaatgttt	180
agtaactgtc	tctgtacctc	tggatgagga	cagctcagcc	gggaatggag	ggggactggg	240
tgaggagacc	agaatgtcag	tgtggccacg	cagcacactt	ttgttttgtc	ttctgtcctt	300
gagcactggc	ttgttcctgg	ataaactagg	cataataata	cctatcctgc	tgtgtgggtg	360
gaagttaaata	gtgataatga	tgtgtgtgag	atgcctgcac	agtgcctgga	ggtattgaag	420
aattattgct	gcctwttctt	tttctacctc	ccacttaccc	gctacccccg	ggtgctacat	480
gttagaaaaac	actgtgtaaa	gtgtggatgc	ttctgaaaaa	tctccctgcc	agcagttagt	540
gccaatagcg	tcagaaaaat	aagatgcaat	gatttggctt	cttttctgtt	tggcaataag	600
aagcttattt	gcmcatagcc	tgatttcttt	caatctgcaa	aaaaaaaaaa	aaaaaaaaaa	660
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	720
rggngngcc						729

<210> 133

<211> 1079

<212> DNA

<213> Homo sapiens

<400> 133

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cttccctttg	tgttaggtc	ttttcttctt	gtgagcttta	gataaacaac	ctagtgttta	180
aacttttttaa	taagggtatc	attttttaat	acatgagaat	tcatttcaaa	attttggttt	240
tagttattta	ttttattcta	cttggtctct	tttcagacag	atgttctctc	ctggattgta	300
aaagtcgaat	tcaaaggatt	tttatttgta	atatacttaa	cctttctctt	gtaagttgcc	360
atctgtgtag	atacagcttt	gattgcctga	caagaggaaa	atgtttccca	ttatcttttc	420
ctgcctgaac	tatacggcca	cttgtgttcc	agcatagtgg	ttcttaacct	tcatagtgtg	480
tcagaatcac	tttgacagagc	ttttaaaaaa	tctagatgcc	tggggaccac	cccaaagact	540
ccatttttgt	gtcatgggtc	aaagcacagt	cttctagtgt	gcagctagtg	ttgagtacaa	600
ctagagttta	acctcgttga	attttagttt	aatcttgggt	ggtcttgaag	atgttagtaa	660
tctctattca	tttttttkga	aaagtaccaa	tgaratcaga	aagttaatta	gaaaacatct	720
agttgaatcc	cctgttttta	atagatgggg	aaaccaagac	ccagagaata	taatccaaag	780
ctacctgtca	cataggccac	aatttctttt	ccaatattct	gttcttctgt	gttcttctaa	840
tttgcagaac	tcctctttta	aaaacctttg	gagaatgtat	tggcctcata	ccctcttctt	900
tcagcctgaa	agacatgcac	ctgtcactta	tttatgatat	ttaaatgcaa	cctctagaac	960
aggggtgtcc	aatcttcttg	cttccctggg	ccacattgga	agaagaaatg	tcttggggcca	1020
cacataaaat	acactaatga	tagccgatga	acttaaaaaa	aaaaaaaaaa	aaactcgtc	1079

<210> 134

<211> 1297

<212> DNA

<213> Homo sapiens

<400> 134

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atccgttagg	tgggtccaacc	ttcctcttca	ggtgtctact	agaggcaagg	ttggatgtat	180
gcggctgccc	tcagtacagc	cccttccttg	ttttttcttc	atltgtgttt	acttaaaaca	240
ttaatccttt	tctccctctc	ctccatccct	ctccctcccc	tactatacag	ttatgactta	300
cactaatcat	tcccgatgat	ctcccagaag	gaaataagtg	tctgtctgtc	tctgtctctg	360
taccatcgtc	ttcttggtac	agttcggact	atlttttctc	tacaccccag	ttatgcaaag	420
tgtagtccct	gaaccagcag	cctcagcatc	ctgagggaaat	ttgttaaaaa	cgcgaaatct	480
caagccctac	ccagamttac	tgaatcagtg	tctgcattgc	aacaagatcc	cctggtaatt	540
cmtatgcaca	tcaaaatttg	gaaggcacag	ctctcaactg	atgtcctggg	tctccttcac	600

atccatcctg	ggaaggtctt	attcctcatt	cctgagctca	tcccactgaa	gagctatggc	660
acttccaatt	cctgagcctt	tgtgaggttc	tgcgtgtcag	taagcttget	tccgggcata	720
acctccgaaa	acacttgggt	ttcagttttc	tctgtgaggc	ttcttaagga	gtggaggaaa	780
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accacgtccc	accgggatac	ataggtttta	cgggtatcctc	tgaacctccc	tttaatcaag	1020
agagtggaca	aaactgtggg	tcccyemtyt	tcaaaatggc	cagtaaaaga	ggaaataagg	1080
atatgcaagt	ttagttattt	tctgetgecc	tctttaagtt	gattggggat	ctctttgtca	1140
ctactttggg	aagataactt	acctttcttat	ccactatggc	taattggagc	ttttctcatg	1200
tctttatggt	tgtcgggaaa	ttttcaaata	aaattcactg	ggaatggttt	gaaattgcaa	1260
aaaaaaaaaa	aaaaaaaaaa	aaaaaatgac	cctcgta			1297

<210> 135

<211> 617

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (9)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (513)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (559)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (587)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (602)

<223> n equals a,t,g, or c

<400> 135

atggaaaaanc	aggcaaatcc	tgaaatgggc	tggaaaaaag	ggaggggaccc	agcactycca	60
gggagaaaaac	ttggcatttc	ttgggaatct	aacaggatgc	agtgaaccca	agccttttga	120
agagctcacc	aatcagactg	cccttgctct	tccatgagca	gatgtttgat	agtattgcgg	180
aggccctcta	gtgggtatgc	tgccaagcaa	ctggagtggc	acttgggctc	taatccagtt	240
gtctatccct	ttcacccctg	catttcacat	gccaaacaaa	aaccaactaa	ctcagaaaaa	300
aaggaaaagcc	cctcaagggt	cctttgaccc	cgatatctac	atagatgcta	tgggggtccc	360
ctgaggggta	ccaaaacraa	tcaaagctcg	aaatcaaata	gctgctggat	tcaagtctgt	420
cctttttcttg	tgtctacta	taaataaaaa	tgtagactgg	ataaattaca	tatactataa	480
aaaaaaaaaaa	aaaaaaaaaa	ctcgaggggg	ggnccgggtac	ccaattcggc	ctatagttag	540
togtattaca	atcatgggnc	gtcgtttttac	aaaqtcgtga	ctggggnaaa	acctggcggt	600
anccaatttta	atcggct					617

<210> 136
<211> 1311
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (1284)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1296)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1301)
<223> n equals a,t,g, or c

<400> 136
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aagaatggct ttactttaca tcgaaacccc attgctcaga gcactgatgg tgcaaggacc 120
aagattggtt tcagtggagg ccgccatgca tgggaagtgt ggtggggagg ccctctgggc 180
actgtggcag tgattggaat tggcacaata cgggccccca tgcagtgccca aggttatgtg 240
gcattgctgg gcagtgatga ccagagctgg ggctggaatc tgggtggacaa taatctacta 300
cataatggag aagtcaatgg cagttttcca cagtgcacaa acgcaccaa atactagata 360
ggagaaagaa ttcgagtcac cttggacatg gaagataaga ctttagcttt tgaacgtgga 420
tatgagttcc tgggggttgc ttttagagga cttccaaagg tctgcttata cccagcagtt 480
tctgctgtat atggcaacac agaagtgact ttgggtttacc ttggaaaacc tttggacgga 540
tgacagtggc ttttctgtga tgacagacas aatggaggag agatctgctt atgggaagta 600
saaccatgaa gtgactgtca cacatgcacg tccaagaaac atcctgaaaa cacatgaagt 660
cgtaaaactgg agaagcagct ctacagcaga gattatctcg tgtttcctct ttctactggg 720
ccagaaaaat cctcagggtt gcagtgtggt gagtgggcag ttgacatatg catgttgcac 780
ccgatgttgt ctctaagtta gcaatgtgtt atttccagct ttaaagggtga gattgtagag 840
atgctgtcaa agggataagg aaatagcaag atttttaagt agtgtgtttg tgaagactga 900
tcccatttta caactgcctg ttctttctcc agtccctttt tttccagcca gcttgactat 960
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tgtatataat atgtgtgtta aaaaaaaaac tgtaaaaaag raaggacaaa caggttggtt 1140
tgttctagtt ctaatttctt aaaaaccact acatgggttac aaaattggaa taacattttg 1200
gggggacaac tgggggttaac taccaaaagaa ggagggtatt aaagaggaga tgggtggttg 1260
attgaccca tttggaataa tttnaggctt acagtnccca nagctgttag a 1311

<210> 137
<211> 1095
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (616)
<223> n equals a,t,g, or c

<400> 137
gatggtatgt gtgtggtgtg tatagggtga atgtgtggtg tgtgaggtgg gcatggtgtg 60
tgtgaggtgt gtgtggtatg tgtggcatgt gtttgggtgt tatgggaata tactatggat 120

taggacatgt	gggttattca	agatctatc	cttttgtgct	ttgaaatctg	atgtgtagaa	180
actgtggcct	cactgaggag	gagttttaga	atatgcaagg	gagatgatca	ggactggatc	240
ttgtattttg	gtaccacatc	cagtcccaga	cagcatgcta	aggcaaggag	ctcataaaaag	300
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ggggagtcct	gatggctgcc	tggttgttac	aggatgttac	agcttaggcc	tggggacata	420
gcccagcacc	ctccagargt	tgtgtctgtt	ctttactctt	caggttccct	ggaggcagga	480
gaggartctgg	cctcatttct	ggcaggcacc	ccactactgt	tattgagcaa	tcctccaggc	540
tgcagagatg	tcagaggagg	accctaattgt	ctockgattt	tgattatttt	gttctttttc	600
cctaggtgtt	ttactngcag	ataccttgag	taccttggtt	gtatattcac	tttgaaagca	660
cacattttaa	tgtttataag	gaaaagggtc	taaagacatc	cattgatcca	ttcattcatc	720
attcagcaaa	tacctgttga	atacctgctg	tgtgctaggc	actgcggtgg	gcgagccaga	780
rggctttgtt	gctccaagga	rcctgcattc	tagtattcta	gttattttca	cgcactctga	840
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ttggcttggg	tcaggctgct	aagtagctga	ggtgaaagca	tgtgccaccc	ctcctgatac	1020
agggatcctt	gctgattgtg	tgtgacacca	gggccttccc	atctgtcagc	tgggtttgtc	1080
ctcacagtag	ctcga					1095

<210> 138

<211> 692

<212> DNA

<213> Homo sapiens

<400> 138

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caaagcaaat	attattatct	taatcttatt	ctgaattttc	accactaaaa	ccacattcta	120
ttgaagggaat	atataataaa	agtgcattat	catatagttg	cacaatgagg	gattcagggtg	180
cgaagggaag	actcattcct	gtgaaaacat	agcccatccc	cagcagttgg	tagaaggatt	240
tgcctggagtt	cctcctcttt	gtgtggccta	taaaacattc	catgaggcat	gtggcaatag	300
tcacaatgat	agtggctctta	tctcctccag	tcttagcacc	ctcactcaag	ccacctcttt	360
tcatagacac	atactttatg	tttggaaga	ggtgctctag	gtgggacacc	cctgcctgct	420
ccaaataatt	cctactgaca	tccatggcag	cttcattcta	tctgagctgg	agatttgagg	480
atcttaggtgg	gcacagaaga	aagaaggggg	ttggggcagt	gtcgttttga	tgattttgac	540
agattcttcc	tgggggtaaa	gagagatagg	tgggtctaat	catccaggga	ataaaatgcm	600
aagggtgtgtg	tatatggaaa	atccaaggga	gaggaaatta	aaattatccc	agattgctta	660
tttaatatgc	aggaaactca	actttccatg	aa			692

<210> 139

<211> 748

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (60)

<223> n equals a,t,g, or c

<400> 139

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ataaggaatg	aatctctggg	ttggccaatc	ccgaactcat	tagctctgaa	ctcccaacac	120
acattcaggt	gcactctgca	tacacggtca	ttctcagggt	atgctcaagt	tattgctatc	180
gggcacatct	gccctacaga	attccagcag	aaatacccaa	tgggagtggg	gggtctggaa	240
acaggaatgt	gggcagagct	gaagctgctc	tcttggggga	gggctgctat	tgtgtgtgtg	300
gtgtgcctga	gaagagtagt	taggggrgga	cacagtccac	cagcaggtca	aggtgggcag	360
ggagttaagg	tccagtggga	aggagtgcag	ggatcaggaa	gtggccagcc	agaagacatg	420
agatgggaga	agctacatgt	gaggattctg	atgcagggca	tgcattggagc	cccacaggat	480

gacatcagat	ctgtccatgg	ctccacagca	tttcttgaet	gcctccatct	accctgcaga	540
cccacctgcc	ctgggggttc	ctttggatct	ggctgaccag	atgcccttgt	gggagcctgg	600
aggctggagg	agagtggatg	gtgagacca	ggcctccagc	tctcaccctg	ccaggccaca	660
gtggtcaggg	ctatcagggt	ctaagcccaa	actgaggtcc	aaggggagtt	ggtgggcagg	720
tggcgggtag	ctggaaaaca	cactcgag				748

<210> 140

<211> 1132

<212> DNA

<213> Homo sapiens

<400> 140

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aactagcagt	gctctctcca	tctctcaggg	cccaaccac	atgggtttcca	gtttctttga	600
ttctctctat	ctcctctttt	attctgctgc	tgctgcttgg	tcagtccctga	atcaaagagc	660
ccttgaaggc	cttttcatac	catggattag	ttaacgaact	ttctctctta	tagaacatga	720
aggatgtatc	actggatagc	taattggcca	attacctgtc	cctgtttaag	tatctttgtc	780
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agggtctctc	atatcctgct	aagttctgaa	ggattccccc	ataatgtgcc	cccacctact	1080
cactacccta	tcctccaatg	tcataactgc	aatagagatc	cacttccatc	tg	1132

<210> 141

<211> 1112

<212> DNA

<213> Homo sapiens

<400> 141

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aaatggaatg	atttatttgt	atcttgaagg	ccaccccat	cttaatgaga	tcctcttcat	120
tctgcacttt	taaagggtat	tgcagcactt	tatcaggcca	gcagcttttg	ggtaatactg	180
tatgtggtag	gaactgtgga	tctttgtggt	catatgctgt	cattgtacct	cctattctgc	240
aaagtggaa	ccttgttcta	agatactatg	tgagttttct	tgtagtgaa	tgagatactc	300
ctatgagtc	ttggatagta	atactgggtc	aggcaccata	gacagcatag	gcaaagtgt	360
atagtagtcc	ccccttatgc	atgattttac	ttctgtggt	ttcaattacc	tatggtcaac	420
cttgggtccaa	aaatgttaaa	tggaaaattc	cagaaataaa	taattcataa	gttttgtttt	480
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aggcatgtgc	caccatacct	ggctagtctt	ggctattttt	atttttattt	ttatagggat	660
gcagtcttgc	tatgttgccc	aggctggctc	tgaattcctg	gcctcaaata	atcctccac	720
ctggcctccc	aaagtgtctg	gattataggc	aaaaactact	gcacctggcc	ctaattcata	780
ggttttaaat	ggtgcactgt	tttgagtagc	acaatgaaac	ccttgagctgt	ccattccat	840
ctggcctggg	atgtgaatca	ttcttcgttt	agtggctcca	cactgtatat	gctaccgcgc	900
cattagtcac	ttaatagcca	tcttgcttat	cagaccaact	gtgagagtat	tgctgtgttt	960
atgttaagta	acccttatat	tacttaatga	ttatccaaag	cacgacagta	gtgatgctgg	1020
caattcagat	gtgccaaaaga	gaaactgtaa	agtgcctcct	ttaagtga	aggtaaaagc	1080

tctcaacaaa aaaaaaaaaa aaaaactcgt ag

1112

<210> 142

<211> 1084

<212> DNA

<213> Homo sapiens

<400> 142

ggtttggggg	catcacagac	tacacccgta	tgagaggatg	aacttaaattg	ataaattgtg	60
tgtgtgtgca	tgcatgtgtg	cgtgcatgtg	gactgtttaca	ctcattgggc	cttctgctgt	120
ctctctccct	ctcctcagcc	ctcttttattc	cctgggacac	agaaattttt	aaataaggcc	180
aattaataat	ectacattgg	tctctttacgt	gttagagtga	aaagaagatt	cacatatctc	240
tcatttttaa	ttgaaagcta	gaaatgatta	agcttagtga	ggaagccatg	ttgaaagctg	300
agatagtcca	aaaactaggc	ctcttgccac	agttagccaa	gttgtgaatg	caaaagaaaa	360
gtgcctggag	gatattttaa	atgctgctcc	agtgaacaca	caaacgatag	gaaagcaaaa	420
tagccttatt	gctgatattg	agaaagtgtt	aatgggtctg	atagaagatc	aaaccaactg	480
caacatttcc	ttaagcaaaa	tcctaattca	gaacacagcc	atagctgtct	ccaattctat	540
gaagacagag	cagagaggaa	gctgtggaag	taaagtgtga	aaataagagg	ttgttcattga	600
gggtataagga	aagaagacat	ctccataaca	taaaagtgtg	agtgaacat	caagtgcgaa	660
tcacagaagct	gcagcaagtt	atccagaaaa	tctaagatca	ttgaagaagg	tggctacact	720
aaacaataga	ttttcaatat	agacaaaaga	gccttctgtt	gatttttaggc	atctagccta	780
aaatggaaga	agatgccatc	taggacttta	atgggtagag	aggagaagtt	gatacctgtc	840
ttcaaagtaa	agactgactc	ttttgttagg	ggctgttgca	gctggtgaca	ttaagttgaa	900
gccaatgctc	attcaccatt	ccagaaatcc	ttgtgccctt	aagaattatg	ctaaatctac	960
tctgactgtg	ttctacaagt	agaacaacaa	agcctggatg	acagcatatc	tgtttatagt	1020
catgggtttac	taaatatttt	aagcccactg	ttgagacctg	ctgctcagaa	aaaaaaactc	1080
gtag						1084

<210> 143

<211> 1050

<212> DNA

<213> Homo sapiens

<400> 143

ggcacgagct	tttcagcatt	tgatgggttg	tgaccactcc	cactttcaca	gaaccttcac	60
caaacagcct	tctatgatcc	caaatgcaac	ttctctatcc	atcttttatgc	tcttctctctg	120
cctactcatg	aaaatgtttg	ggccatccag	gcttccattt	ttagccctca	ctttgtgcag	180
gtttataact	tattttcagt	tttgttatct	gatctctgac	tccagcccag	accattcctg	240
actccacatc	cacatattca	tctggcttgc	tgaataactt	ctcttggatg	tacatgtgtg	300
ccttagactc	attatgtgca	gacatgaagt	catctttttt	ctctccagac	ctgcttttcc	360
tctcgtatcc	ttcttttttg	tgaatggtac	aattatttcag	atggaacgtc	caagtcaaaa	420
gtcgtttctag	aatcctccct	cactcctaatt	gccacatcca	attagtgcac	aaatcctatc	480
gattcggcct	tctaaataca	gtcaaaaacat	ttcattcaat	tcagcgtcac	tgctattgct	540
ttaatgtaga	ccttctctat	tttaccatga	tcaagcagag	gccctgtatc	tatattcttc	600
tgcttccag	tcttgctatc	ctactccgca	gttaatcccc	tgagtgcctat	cctagtgtac	660
cttctaacag	tacagatttg	gtcatggatt	ctccagcttg	aaataacttca	tgtcttttgt	720
gggaacatgg	atggagatgg	aggctattat	acttagcaaa	caaatgcatg	aacgaaaacc	780
aaataccaca	tggtcttact	tataagtggg	agctaaatgc	tgacaactca	tgaacacaaa	840
caaatgaaca	gcaaacactg	gggtctactt	gagggtggag	tttgggagga	gggagagaag	900
cagaaaaggt	aactattggg	tactgaactt	aatacctggg	tgattaaata	atctgttcaa	960
caggccccca	tgatatgagt	ttacctacgt	aacaaacctt	cacatgtatc	cccaaacctg	1020
aaataaaaagt	taaaaaaaaa	aaaaaaaaaa				1050

<210> 144

<211> 1113

<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (349)
<223> n equals a,t,g, or c

<400> 144
gttggtgttg agcacagctt taggcttaga ttcttcatca actaggagaa gctgtgcttc 60
aatcacagtta ttcgtttgca tgggttctaa tgtgcttcac tcaatttagc agaatttttt 120
ttttaacctc ttcttgacg ctactgtgct gtgcaaatca catcttgagg ccctactctt 180
cttcacttgc tgacagatgt gtaggtgaga aaagtctcat agtcattgtt cctgaaagaa 240
gcttccagac ccacttctag ggccagtgc atatgcagga aatcagctgc ttctgggcca 300
ggacagagct ggtctttttt ttagtggggg atggcgggca gtggggcang ggacattcaa 360
aatttatatt ccaacagaca gatagcatca gcaggtacaa ctacaagggt atctacatag 420
atcatacatt cacaaggcat tattagtcca acagtgcaga agccactcgt gggttttctg 480
taacaatatc ccacttcata gtgtaaacag gtactatttt gttcacttac aattccggaa 540
ggaaggggcac accttgacg ggggaagaaa aggggaatcc taaagtaagg tgcaacaatt 600
aagagacaac actttggcta acaatcttgg atccacattt cagtcagggc ctccacata 660
gaggggaaaag acttttctct cagaagttag aatctttctt cctcctttct tgttaaactg 720
agagcagtgt tttgtttgct caatattaca tgtacaaaag gagattagaa gaaaatgcat 780
cacaaaacca tcttgaacgt tcagctcttc ctgccaatat atcacaaact ttaggtttta 840
gacggggcct gggaatacgt aagtgttttt tctttttttt ttttttaagt gaaagcaagt 900
ttattacgaa agcaaaggga taaaagaatg gctgctccat aggcagagag cagcccagta 960
atcttaaaat aggaaaatag acactatggc tacaaaaaat aaaaaataaa tgaggtagat 1020
aaaattttca caccaggac ttgcctgttc caacttcata gtcttcatga aatattcatc 1080
aagaagacaa aaaaaaaaaa aaaaaacctc gta 1113

<210> 145
<211> 685
<212> DNA
<213> Homo sapiens

<400> 145
ggcacgagca ctctctgaaa taaaagggag ccgcttaca gaaataaatg atgtatgtgc 60
aatctgctat catgagttta caacatctgc tcgtattaca ccgtgtaatc attatttcca 120
tgcactttgc ctctcgaaat ggctgtacat tcaagatact tgtccaatgt gccatcagaa 180
agtatacatc gaagatgata tcaaggataa ttcaaagtga tctaacaaca atggatttat 240
tccacccaat gaaactccag aggaagctgt aagagaagct gctgctgaat ctgacaggga 300
attgaacgaa gatgacagta cagattgtga tgatgatgtt caaagagaaa gaaatggagt 360
gattcagcac acaggcgcag cagctggaag aatttaatga tgatactgac tgatgaaaat 420
agcattttat aatgattgag gtatttgttt aaaattcagt tcatccaaaa tggagtaata 480
tccttcacct tcagtgtgta accaagcaca aaaacagtat caatgttgaa tctgtgaatg 540
gttttccggt tactgtgatg tgctactgta aatatacctc tttaattact tctggtctct 600
ttggtgacct gtttaaaatt gtgtacatta ttgtacatag aataaaatgt tttcacattt 660
ttatgacaaa aaaaaaaaaa aaaaa 685

<210> 146
<211> 1038
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (743)

<223> n equals a,t,g, o,t,c

<400> 146

ggcacagtga	agccatctat	tgacaaatgg	aggagaatga	tgaaaagttg	taagatgttt	60
aaatatatttg	ctattattca	tgattattcc	taaattttat	cttttcaaac	tgttgctact	120
acttcagaag	attacacatt	ttatctgtgg	caagacactg	aacaatttaa	attttaggtg	180
tgaatcatat	ttcctgtttc	tgtacctcta	ttgtgcatac	atattatact	aattcttaac	240
aggaaaaaat	acttttttck	tttttatctt	tgtacttttt	tttgaaggtt	ttaatttggt	300
ttagagatgg	aataaaaaag	ctgtgatgat	atataatcct	aataataaaa	ttacttgatc	360
aacgggtttg	aaaaatatcc	ttwaaaaata	atagggcatg	gtggctcata	cctgtaatct	420
cgtacttttg	gagggcggaag	tgggcggatc	acctgagget	ggtcttgaac	ttctgrgctc	480
agacaatctg	tccacctcgg	cctcccaaag	tgctgggatt	acaggcatga	gcccactgca	540
cctggctggt	atgtcctttt	gatgaatcaa	ctctttcata	attataaatg	actcttttta	600
tccttggtaa	tgtcctttgt	atagaaatct	tttttttttt	tttaataaag	aaacagagtt	660
ttgctctgtc	aggetggagt	gcagtgggtg	agttataact	aactgcagtc	ttgaactctt	720
ggccacaagt	gacccctcctg	ccnyggctca	tacctgtaat	cccagcactt	tgggagggcg	780
aggtgcgcgg	attgtctgaa	gtcaggagtt	tgagaccagc	ctggccaaca	tggtgaaacc	840
ccatctctac	taataatata	aaaattagct	gggcatgggtg	gtgggcacct	gtaatcccag	900
ctactcagga	ggctgaggca	ggagaattgc	tgaaccgcgg	gaggcggagg	ttgcagtga	960
ccgagatcac	accactgcac	tccagcctag	gtgacagagt	gagactctgt	ctccaaaaaa	1020
aaaaaaaaaa	aaactcga					1038

<210> 147

<211> 851

<212> DNA

<213> Homo sapiens

<400> 147

ggcacgagaa	caaattgata	gtgagcatta	agggtttcca	agttggattt	gtaactcctc	60
atcattcctt	gtatgacaac	ttcttgaata	tatgtcacta	tgtagtataa	ttaaacactc	120
caaactcatc	ttctgtttgt	tagaagtttt	cagcgggtact	tccatgcaac	tttaaactctc	180
actgctctct	atgggttgatg	tcaaattgacc	ttcagttaatg	actgagaatt	gaatacaaat	240
agattacaaa	gccaaaattt	gatgttaaat	gactcaggaa	attttagttg	tattttcaat	300
tcaagtactt	agtagcctac	gtttgctttg	cctctggttc	tttatggaaa	ataggccttg	360
tagtggcatt	gtggagcaaa	ggagactgtt	acaccttaat	taactttttt	tactgatgca	420
aataatttga	ggatagagag	gaggggaagta	gtgaaagcta	tgacctaaaa	cattggggacc	480
aaatagaggc	tcacagatat	ttggattatt	ttatgtgctt	attattaaat	aaggaaagca	540
ttttgtgata	tgtggaagac	gctatgtgaa	gttttaccta	tcttctcaaa	gaccttttct	600
tttgtatttt	cttttggtgt	ttcttaaaagc	caaacaaaga	aatgtttctta	aggagacagg	660
gtgggttttt	ctgtgggctt	ttgttggttt	ttctgtkggc	catcgccctc	taatggaatt	720
gatctctggc	tgtttgattt	ttttcatatt	gtatttttaa	aatttgttgt	acagtgcctt	780
gtgagacca	agtaccacta	gatgaataaa	acgtattata	tctaaaaaaa	aaaaaaaaaa	840
aaaaactcga	g					851

<210> 148

<211> 614

<212> DNA

<213> Homo sapiens

<400> 148

ggcacgagcc	aatatccact	ctaccagct	gggccccag	tctacaaccc	tgcagctcct	60
cctccctata	tgccaccaca	gccctcttac	ccgggagcct	gaggaaccag	ccatgtctct	120
gctgccccct	cagtgatgcc	aaccttggga	gatgccctca	tcctgtacct	gcactctggc	180
ctgggggtgg	caggagtcct	ccagccacca	ggccccagac	caagccaagc	cctggggcct	240
actggggaca	gagccccagg	gaagtggaa	aggagctgaa	ctagaactat	gaggggttgg	300
ggggagggct	tgggaattatg	ggctattttt	actgggggca	agggagggag	atgacagcct	360

gggtcacagt	gcctgcttc	aaatagtc	ccctctctcc	tctgctccca	agatccagc	caggaaaggc	420
tggggcccta	atgtttgtcc	cctctgggct	ggggtggggg	gagggaggag	gttccgtcag		480
gcagctggca	gtagccctcc	tctctggctg	ccccattggc	cacatctctg	gcttgcctaga		540
ttaaagctgt	aaagacataa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa		600
aaaaaaaaaa	aaaa						614

<210> 149

<211> 1200

<212> DNA

<213> Homo sapiens

<400> 149

ggcacgagga	gagagaagat	gatgaaaaga	ctgttgatga	ccgaactgtg	aaattctccc	60
cttgtcacct	ggaagatggc	atgggtgcctt	ctgtccgtct	tctttcttcg	ggcttttgtgt	120
gctcactcta	gcacagcata	caagtgtgtg	ctttgttcgc	ccaggtctcc	atggttagtt	180
gaagccaatt	tctggcttga	cttttatggg	aaaagttatt	ttatgtctcc	taagcattag	240
agtttttcta	ttactctatg	tagttgagac	aggatttgat	aagtctagga	aaagaaagat	300
gggaaaacgg	gattcccttt	cagaagtacc	tgtgtgtatc	tgtaataaac	cacaggggtt	360
aatatgatgt	aggatctttt	actatcaatt	tcaaccattt	gattttgtat	gattgaaact	420
tgcaccgagc	tttgactggt	tgtaaagag	tcatttttaa	tgaaagaata	attctttatt	480
gctggttttt	catttacact	gataaataca	cagatcttaa	taaagtcttt	aacattcatt	540
tgtattcaga	tgtgagtaga	agaactaaaa	aaagaaagtt	acatatcact	atgactgaag	600
gtacttcagc	ttaatctgaa	atataattta	acttgtgaac	tccttgata	tgatattatt	660
tggaataaac	agaattttatc	attgaacccta	aagtaggaaa	tgatagctta	cattgtctaa	720
aaatccttac	aagggttaaga	tgattcaata	tcaagaatat	tcagaaaatt	atttctaaag	780
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tagtttcaag	aaatgtgttt	ttaaattttt	attaatgcac	ttgaacaact	ttgcaggaat	900
aaagcaaccc	cctaaccaca	aaatatccct	ctaaattagt	tccttagctt	tctcaatgaa	960
tacacacata	tttttacata	gctatgatcg	ttgtgtacat	tctcctttgt	tttacttctc	1020
ggcctaacac	ttgtctcttc	ttgtcaacac	agattctact	ctcaccaatt	taaatgtctt	1080
tatatccatg	ttacatgggt	aacctcactt	cacccatta	ttagatattt	gagttatata	1140
taatttttca	ctcttataaa	tagtgctgct	atgaatgtct	gtaaaaaaaa	aaaaaaaaaa	1200

<210> 150

<211> 683

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> n equals a,t,g, or c

<400> 150

gggagaatag	gttagaagaa	aatatctacc	ctgagacagg	naaaaaacaag	aaaatgacat	60
atacagaaaa	gagcatatga	gacacaggaa	ctggtagtaa	agtctatgaa	aggctgttgt	120
ctctcaccta	gtgttgggcc	taaagttgct	gcagtcagaa	aggcctgcag	ttaaaaggaa	180
aagttggatg	tcaagtggga	aatactgaga	agaaaagttc	tcagaggaag	caatatcctc	240
cctaaaaacc	aggaactttc	gaacaactca	agggtccact	ttcaggtcaa	gtgctgaaag	300
gcaatgcaga	tgacagttgt	atgggtatgtg	attactgcaa	tcatttggtg	gagaatgagc	360
atgtgtgaag	ccctctcaca	gaattgcttc	taatcctaaa	atgtatctca	ctgtgatgaa	420
aaacaatcaa	agtacagttt	agactaaggg	atgtgtcctc	aagtttagca	gactcttaaa	480
cacttacttc	tagttgtagc	ttgattatct	cattttgttt	ttctttttct	tgacttctta	540
gctttgcatt	taactctgaa	atttccatct	cctttttctc	tattagttct	ttgtgctttt	600
cttcatttaa	ttcaactgaa	taaaatgaaa	taaataaaat	tcatttggtta	aaaatttcaa	660
aaaaaaaaaa	aaaaaactcg	tag				683

<210> 151
<211> 827
<212> DNA
<213> Homo sapiens

<400> 151
gggcacgagc ttgggcctca agtgattctc ctgccctcag cctctcagga caaccccgagt 60
tctgtcatcc acgtggtgaa tcagaccaat gcccaaggcc agcaagagat tctytamtat 120
gtgctgtctg aagcggcagc agcctcccc agcccttgag ccaccttcag ggggcacatc 180
ggaaaagctt caaggaatag ctgaggagcc agagatccag atggtttgaa ggccgcagag 240
ccagaccatt tcttccccag gtcttgaagt ttgagccagg caagtggcag tgcccttagt 300
gggcagccgt tgccaatgga tgccttttagg agtgggtgcc agagcagtgt ggtccactct 360
ggcctggggt tgcattcatc tgcagactct aaagacttcc cttttctgcc agactacatt 420
ttgtggggag cctgaggact ctggattctt tgaggggagc ctggatgtgt gtgttcttgt 480
taaagaggct gttatcaggc ttaaccataa cctcaagat ctgcttgaca gtgattaaat 540
ccttagctca catccattcc catctttcgg gctccttagg cccaaggatg gcatgtgact 600
ggtccttgca agggtccttt ctttgtcacc agccaaggca ttgataacca agtagccatt 660
ttcctcttaa gggttctctt acaaccccaa ggactttcat gattatcttc agggacagga 720
ttggagggar tgagcgtgtt tattaacaaa ttgtttttgg taataaaata aatgcttgga 780
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 827

<210> 152
<211> 835
<212> DNA
<213> Homo sapiens

<400> 152
aaaatatttt ggtagtaatt taaaatacaa gaacgaatat ttatttgtcc acagttggag 60
atgttggata aatgtctttt ctcaaagatc acaggacttt tgtctttcat ttttgcttt 120
ttatttacca ttataaaaag atctggtctg gattatggaa tttaatgttt atcagctcta 180
tgtattcctt tatagaggct tgaggaagta ttccacataa catgttttat aatacttaac 240
catttatcca aagatatatt tacattgggt tgtgccctt tcccttagat catggtaaat 300
ttttcttatt gaggttaatta tgtactactt atatttgaag gaagcttatg acattttaca 360
gtagctaaaa tgttgagatt agaggactt ttactattct tctcaaagg aactgatcag 420
ataattaccc aaattattca agaaaataga tcagaaataa agaacaacat aattttctaa 480
gaattcattg aaatttatgg aatcagctct cgcactgcc atctttgcag ttttgaaaaa 540
gaaattgctt aatcacaaat gttctacagt ctttaaagt agtagaatta gacagtgaga 600
tcacttgagt aaattgattg gtgattccag agataagact aatattttta attatttatg 660
atactgatta gtataaaaaac gtactcatca cagaatttga agcaaaatac atgtacactt 720
caaagagtaa atgacaaatg tataaatgct gtagctcagg attatatgta cctttaaaaa 780
tacactaata aagattattg ttcaaaaatt aaaaaaaaaa aaaaagggcg gccgc 835

<210> 153
<211> 558
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (27)
<223> n equals a,t,g, or c

<220>
<221> SITE

<222> (39)

<223> n equals a,t,g, or c

<400> 153

cgggaccgga	taacaaat	taacaaat	cacccengga	aacaggctnt	gccccactag	gcttttggca	60
aaaaagctat	tttaggttgc	cacttttagga	ggtacgcctg	gcagggtaccg	ggtccggaaa		120
ttcgcgcccg	cgtcgcgactc	atgactgtgt	tggcacttta	aaaatattga	tatcccacaa		180
taaacagggg	tatcattgat	ataatttccc	acatatttta	ctataaataa	tcgagtaaca		240
acctgtcttg	taccattctt	tacagaaagg	cttttctcaa	tgcgttagtc	agggtttctt		300
cccggggaga	aaattttataa	tccttaatga	ggccagtact	cagaaggaca	tttctgctta		360
ctcttttctc	tgtaattgcc	ctcactaaaa	taaagcatga	ctttttttatc	atgtgttcac		420
acatgcagtg	catccctaga	gtttttctga	agcatgaatt	caataacata	taattagacc		480
tgattctgag	aagattttct	cttcttcgtc	gacgcggccg	cgaatcccg	gtcgcagagc		540
tcactagtcg	gcggccgc						558

<210> 154

<211> 1201

<212> DNA

<213> Homo sapiens

<400> 154

ggacatttgt	aaccctataa	acactagtaa	attaaaaaca	gaaggacctt	tatgtcctaa	60
catatctgtg	ttgtgaaagg	ctgccctgtg	aaatacggga	tttcttaaac	atatttttaa	120
aatcataggt	gtcaatattt	tttagaaatc	catttaaatt	ttctcttggt	attttacaat	180
gcctatttat	ttatatagtg	gctctgctga	ttttgatgta	tatcctaaag	tttatatttt	240
ctttaaagga	tgttttatac	aactttatgt	aaaatgtttc	agtatcttca	cattctctcc	300
ctgtcccttt	gttttgctct	tatatgggtg	tctgagtcct	ttctctggct	ttcaaacctt	360
gtaagactaa	gacactaaag	taactttgcc	cgagggtttg	gtaatgcctk	cyaaakcaca	420
tectaagctc	tcgtgcatac	aggggcctcc	tttgagctct	gtgcttttga	gateccatac	480
acctaaattc	cagtactcca	aatcagtact	gtcagttttt	agtgactaag	tttaaaaatg	540
tatttttaata	rcaagtttagt	ttagtgccct	cttgcttctt	tctcgactgc	ttgtatacat	600
gtatatctct	ttaaatgaat	cttggaattt	atttagaaat	attaaattat	actaatgaaa	660
ctgtatattg	ttgkgaattc	ataagtgaat	ttggaaagaa	tttgtcttta	tgaaactaaa	720
tcctttttat	tcaagaatca	tatgtgtctt	tatatattat	ccagtctaca	tttatatcac	780
tgagtaaata	tatagaaatg	tggatacata	cagctgtagt	tacagatata	aataragata	840
taacctgtta	aatctatatc	tatcccatat	aacatatata	catgtaatat	gtgtgtgttt	900
atatatatat	gtttatgtca	ttaaagagct	cccttaatat	ttttctttta	tttcccttat	960
aatttgaggt	tgagcttgaa	ttttccttgt	ataaacaagc	aaatatttat	actagtttta	1020
atactgatgt	ttagacattg	tatcttattt	tagcgttgaa	tattttcaca	attattataa	1080
atattatcta	atactaataa	tgtacctgtt	aaaaatattt	aaaaattttac	ctttgaatta	1140
ttttattggt	gaattaaaat	tcctttaata	tgataaaaaa	aaaaaaaaaa	aaaaactcgt	1200
a						1201

<210> 155

<211> 1026

<212> DNA

<213> Homo sapiens

<400> 155

gtctaaatgt	tcagtttttc	ttcctaattc	caatgattct	cctcatttct	caatgtcctt	60
tgctccatct	tgctgtccca	tttgactgc	ctcccaaagg	tcactgtggc	tccttctctg	120
acttccacag	tcaagttaca	cttcataaaa	attctaagct	cattttcaga	agccacaaat	180
ctatecttct	ttaaagtctt	caaactttga	ttgtgtaaat	aaatactcag	aaacaagatt	240
tctaaaaaac	aaacactatt	ggccatcgta	tgttcaaagg	agataacaaa	tgtttaacct	300
tatatgttgt	aggctttcta	aacttaattt	caaaaaaaga	ctaaataaac	agtgtcaata	360
tgtctataaa	ctcacaacga	aaattttcag	atcatccaat	tgtgtattca	ttggccggaa	420

acaatcatgt	aaaaaccaca	gctctggagc	tgggtagcat	agaaacaaga	atattcagca	480
tttcatgggt	ggtgactcaa	atctctaaag	ggktgtcagg	ttaaaaaaaa	aaaargaaaa	540
gaaaagaata	gaaatttgac	ctgatctata	aaaatgaaag	tcgctgggca	aagttttggc	600
ttttcactcc	tgacaaagat	gagctctctc	ataggtagac	caaggcacac	gagtgtatgac	660
tttcgtggcc	ccaaaattct	tcaagaaaat	agtagattga	ggaagcgatc	tgcgcattga	720
tagagggtgct	gtttgaactg	gatgacattt	aagcttcctt	ctttctccaa	gattctgtga	780
ggccatgaag	catgctattt	catccccact	ccaattgctg	tctccctggc	ctgggtgccct	840
taccacctca	atcttgggtc	actgatctct	tttgcaagaa	atcagtcctg	cctaccacct	900
gcaacttcat	cttcctaaaa	tgtcactttc	cttaaggcct	gctctgttca	aaggccagtt	960
cccagccaca	ccaatgtaaa	ctcgtgccga	attcgatatc	aagcttatcg	ataccgtcga	1020
cctcga						1026

<210> 156

<211> 904

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (8)

<223> n equals a,t,g, or c

<400> 156

accacacngt	cgggagtata	cttaattttta	tttatgtata	gaatatttgt	atttattttt	60
tggacatata	tttatcactt	tgtcattttt	tttaaccaat	ttgagaaatg	ttagctgctg	120
aattaatttg	ttgcccagac	cttcataattt	tcttcttttg	tgccttctcc	ctgtggcaat	180
gtactgttct	cacaatgcct	tttaaaaaatg	ttccatactg	tattagcatc	cttagaaggg	240
acagaactaa	gaaatacat	gtcacaataa	tattttactt	tattgataat	gacaaagaat	300
attttttaaa	cccatcaaaa	atagatttca	attgactgtt	tccctacat	cttttgagcc	360
acagtcgccc	atcgaataag	caaatttggt	tttgagaata	aactggtaac	cagtttgtga	420
tgactctcag	aagccttttg	gctgggatac	agaagagttt	ctaagttcct	agagagccat	480
ttaataatta	gttgggtgag	cagaggcttg	acagagctgt	tacttatgtg	tgagggtttt	540
attctcaggg	agtagtttat	tcatcatttg	gtaagccctt	ccccacactc	ctctaattta	600
aacaagtagt	gaaggcttat	cttaaaactgt	gtagtacctt	agacttggca	tttatttttg	660
atagagcaga	gataaaatat	tttgatggaa	ggaaatcaat	tttctgtaac	tgatgatgtg	720
aaaattttat	tttctgggaa	atttatatag	cattcaaaaa	ttcaaagtat	gttattatga	780
ttggttacaa	gagaataaat	ttacatgttt	aattgttaata	tttgtctcct	atcattttct	840
tccctttcag	tcataataaaa	tgattttacaa	aacccaaaaa	aaaaaaaaaa	aaaaaagggc	900
ggcc						904

<210> 157

<211> 916

<212> DNA

<213> Homo sapiens

<400> 157

gtttgtgtaa	ccatgttctt	cagaatgcag	gtatgtgagc	atcatggttt	ctgggtaatt	60
ctgctgctcc	tgtctttgaa	aatggagata	ccacttgcag	cttatcccac	tgctgagtat	120
tccagcattg	gtagtggttt	cactccattg	catccatcca	gaactttcac	acaggcctcc	180
ccattaccca	gcatttttta	acattgatca	ataaggccta	taaccagatt	taggctagca	240
acaccagagg	tctgggggca	agggtggaaa	ttgactttac	attcttagta	gctaattatc	300
cataagtgtc	ttatatatat	attgttggtt	ttgatcatct	attcaaaaaa	tatatattga	360
gcagctgctg	tgggtatagg	tctgtgctgg	ccagtgaaga	tacatgatta	acaatgttgt	420
gcttgcttgg	ttcacagctc	tgtgggtaca	tgggtggagta	aaataagtac	aattaatttc	480
tcagagctgt	gcacagcaac	acacagaagg	agagataact	cacccagctt	cagaggggtg	540
ggacagagaa	tgaggtttag	ctcccagatg	tccttgtgtc	agtttttagt	gtttttcaggt	600

gttgataaaa	gctccaggag	ctggcaggag	gagagcagag	gaagctagag	cttacaaaagc	660
acaaaggcca	tgacagcatg	ccagacgggt	gaaagaggac	aggggaaatg	taggcaagtg	720
tctcttctca	gaggatgtta	tatactatgt	ttaaaagtgt	tgatctgctg	ggcacagtgg	780
ttcacgcatg	tagtgtcagc	actttggggg	gccaaagggtg	gaggattgct	tgagctcagg	840
agtttgagac	cagcctgggc	aacatagtga	gaccccatct	cttaaaaaaa	aaaaaaaaaa	900
aaaaaagggc	ggccgc					916

<210> 158

<211> 921

<212> DNA

<213> Homo sapiens

<400> 158

ggaactgctg	ctcatggaac	tggctcctct	cctcttgcca	cttgagtctg	ttcgagaagt	60
ccagggaaga	acttgaagag	caaaatacac	tcttgagttt	gttgggtttt	gggagagggtg	120
acagtagaga	agggggttgt	gtttaaaata	aacacagtgg	cttgagcagg	ggcagagggtt	180
gtgatgctat	ttctgttgac	tcctagcagc	catcaccagc	atgaatgtgt	tcgtaggggcc	240
tttgagtgtg	gcgattgtca	tattctgttg	gataacaatg	tattgggtgt	cgattgtcat	300
ggggcagggg	agagggcagt	acacctggag	gaccatthttg	tcacatcga	caccatcagt	360
ctgctcttag	aggatgccct	ggagtattcg	gcgttgattg	cggggcacc	gaaatcagac	420
ttgccacctg	gactgtcgag	gtgcagaccc	tgggagcacc	actggcccat	ctcttacaca	480
ggctgaccga	tttctcctgg	tgttcagagt	ctgtttttgt	ctagcaccat	ttgaaatcgg	540
ttatgatgta	gggggaaaag	cagcagcctc	gaagcctcat	gccaaactctg	ggcagcagca	600
gcctgtgggt	tcctggaaga	tggatgggca	gagaataggg	aaggaagatc	atgcttttcc	660
ctactaactt	ctgtaactgc	atgtatgata	cattattgca	gaggtaagag	atagtthaat	720
ggatttttaa	aaacaaatta	ctataattta	tctgatgttc	tctagttgca	ttttgctgaa	780
atgtagtgt	gttctaaatt	ctgtaaattg	attgctgttg	aattatcttt	ctgttgagaa	840
gagtctattc	atgcacccctg	accttaataa	atactatgtt	cagttaaaaa	aaaaaaaaaa	900
aaaaaaaaaa	agggcgggccg	c				921

<210> 159

<211> 804

<212> DNA

<213> Homo sapiens

<220>

<221> SITE

<222> (800)

<223> n equals a,t,g, or c

<220>

<221> SITE

<222> (801)

<223> n equals a,t,g, or c

<400> 159

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cttcacaggg	ccgctgagtc	acttcttctca	cttcttcattg	gaacattgga	tccctcctga	120
gggtccccctg	gcagggctca	ggaggcttct	cctggaccgc	ctcgtctttg	caccggcctt	180
cctcatgttg	ttcttctca	tcatgaactt	tctggagggg	aaagacgcct	cagccttcgc	240
cgccaagatg	agggggggct	tctggccggc	gctgaggatg	aactggcggg	tgtggacgcc	300
actacagttc	atcaacatca	actacgtccc	tctgaagtgc	cgggtgctct	tcgccaacct	360
ggcagctctg	ttctgggtatg	cctacctggc	ctccttgggg	aagtgaacgac	cgctgggaga	420
acatcaggtg	cactgtggac	gtgggtctgg	gggtctcacc	cgcccagcga	gagcagaacc	480
aatccagtc	ggatgtcact	gactctaaat	caggtgattc	aagatgcccc	aaaatgatgg	540
atagagaaac	agaaatctct	gaatgtcaga	accctgtctt	ttaaaaaggc	agtcrcctgcc	600

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ttcaggtggt gctgccccag aaacttaaaa tttagtcgag gcagtttcaa cgttactgt      660
ggaccgaatt aggatcacaa taaacgataa tgcaggttct tcaaaaaaaaa aaaaaaaaaa      720
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaactc gaggggggggc ccgtacccaa      780
tcgcctgat gatgatctgn ncac                                         804

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<210> 160
 <211> 24
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (24)
 <223> Xaa equals stop translation

<400> 160
 Met Tyr Gly Cys Val Cys Val Cys Ile Tyr Leu Tyr Thr Cys Ile His
 1 5 10 15

Gly Cys Pro Cys Val Ser Met Xaa
 20

<210> 161
 <211> 113
 <212> PRT
 <213> Homo sapiens

<400> 161
 Met Gly Ser Trp Cys Ile Cys Thr Leu Leu Leu Leu Thr Asp Gly
 1 5 10 15

Gln Gln Gly Phe Tyr Pro Gln Pro Phe Gln Ala Ala Pro Gly Arg Gln
 20 25 30

Gln Leu Trp Gly Gly Thr Asn Pro Trp Ala Val Leu Ile Pro Glu Ser
 35 40 45

Phe Leu Pro Tyr Thr Leu Thr Val Asn Tyr Ser Pro Ser Cys Asn Phe
 50 55 60

Glu Phe Tyr Leu Pro Lys Met Arg Leu Ala Tyr Ile Cys Met Ser His
 65 70 75 80

Ser His Cys Pro Tyr Leu Gly Arg Asp Ile Ile Ile Thr Leu Leu Asn
 85 90 95

Tyr Cys Ser Ser Phe Leu Ala Glu Leu Leu Ala His Leu Val Tyr Ile
 100 105 110

Ala

<210> 162
 <211> 45
 <212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (45)

<223> Xaa equals stop translation

<400> 162

Met Thr Lys Arg Arg Lys Pro Arg Tyr Arg Phe Ile Phe Ala Leu Tyr
1 5 10 15

Ala Leu Arg Leu Val Phe Leu Phe Arg Ala Val Thr Asn Thr Asp Ala
20 25 30

Ser Arg Leu Arg Ala Lys Arg Gly Glu Cys Pro Tyr Xaa
35 40 45

<210> 163

<211> 59

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (59)

<223> Xaa equals stop translation

<400> 163

Met Thr Glu Gly Leu Leu Ser Ser Leu Ser Leu Leu Leu Tyr Leu Leu
1 5 10 15

Thr Trp Leu Leu Met Leu Ser Lys Lys Leu Tyr Val Gln Met Ile Phe
20 25 30

Cys Tyr Asn Pro His Phe Ser Gln Met Asp Ala Cys Asn Gly Thr Ser
35 40 45

Gln Lys Ile His Asn Ala Arg Gln Cys Thr Xaa
50 55

<210> 164

<211> 118

<212> PRT

<213> Homo sapiens

<400> 164

Met Cys Tyr Leu Leu Leu Leu Leu Ile Gln Thr Ala Glu Leu Leu Ile
1 5 10 15

His Pro Gln Gly Leu Gln Ala Val Ser Asn Gly Glu Ser Ala Leu Lys
20 25 30

Gly Thr Arg Pro Thr Phe Ser Ser Pro Phe Ile Leu Val Thr Glu Gly
35 40 45

Arg Lys Glu Trp Glu Gly Val Phe Leu Ser Ser Gly Trp Lys Gly Asn

50

55

60

Thr Leu Ser Asn Tyr Tyr Ile Ser Leu Val Phe Tyr Tyr Ser Arg Ile
65 70 75 80

Leu Gln Pro Tyr Phe Tyr Cys Leu Trp Gly Lys Leu Glu Met Val Thr
85 90 95

Leu Ile Arg Ser Val Trp Arg Gly Ile Asn Gly Gly Asp Lys Ile Ser
100 105 110

Val Gly Phe Gly Lys Cys
115

<210> 165

<211> 55

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (55)

<223> Xaa equals stop translation

<400> 165

Met Cys Ser Gly Leu Leu Ser Met Thr Phe Ser Phe Leu Leu Glu Phe
1 5 10 15

Cys Ser Val Ala Gln Arg Leu Arg Leu Ala Asp Ala Arg Thr Ser Met
20 25 30

Gln Asp Ile Leu Lys Trp Phe Ser Asp Tyr Thr Leu Arg Ala Asp Ile
35 40 45

Ser Lys Ser Arg Asp Leu Xaa
50 55

<210> 166

<211> 127

<212> PRT

<213> Homo sapiens

<400> 166

Met Gln Gly Ser Asp Ala Gly His Gly Gly Thr His Ile Tyr Arg Ala
1 5 10 15

Leu Val Gln Trp Pro Leu Ala Trp Val Phe Tyr Leu Ser His Ala Lys
20 25 30

Thr His Trp Gly Glu Glu Leu Arg Phe Ser Phe Arg Arg Lys Asn Leu
35 40 45

Arg Leu Arg Glu Ala Met Arg His Glu Thr Cys Gln Val Thr Gln Leu
50 55 60

Val Ala Gly Lys Ala Asp Ser Asn Leu Cys Leu Arg Asp Ser Glu Thr

65

70

75

80

Trp Phe Trp Pro Pro Leu Trp Ala Ala Cys Ser Ser Leu Gln Ala Thr
 85 90 95

Ala Cys Arg Leu Ser Ser Pro Ser Lys Gly Leu Gly Ala Ser Arg Glu
 100 105 110

Cys Pro Trp Leu Ala Ser Gly Arg Ala Ala Leu Val Ser Phe Leu
 115 120 125

<210> 167

<211> 56

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (32)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 167

Met Gly Val Glu Gln Tyr Ser Tyr Leu Phe Leu Thr Cys Val Phe Met
 1 5 10 15

Cys Val Ser Leu Gln Trp Lys Ser Thr Gln Pro Trp Val Gly Asp Xaa
 20 25 30

Thr Cys Met Arg Lys Gly Ile Thr Gly Thr Glu Val His Arg Thr Asn
 35 40 45

Ala Leu Phe Thr Phe Trp Cys Ser
 50 55

<210> 168

<211> 73

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (73)

<223> Xaa equals stop translation

<400> 168

Met Pro Ser Ile Arg Leu Gly Leu Ser His Leu Phe Leu Thr Ala Gly
 1 5 10 15

Ile Tyr Cys Leu Leu Leu Cys Ala Arg Cys Cys Ala Leu Gly Arg Gly
 20 25 30

Thr Ala Trp Ala Ala Cys Pro Gly Gly Ala Cys Gly Leu Met Gly Glu
 35 40 45

Ala Asp Pro Ser Pro Pro His Cys Gln Gln Gly Gln Gly Lys Ser Thr
 50 55 60

His Arg Gly Leu Ile Pro Tyr Val Xaa
65 70

<210> 169
<211> 70
<212> PRT
<213> Homo sapiens

<400> 169
Met Thr Pro Gln Asn Leu Arg Phe Thr Leu Phe Gln Phe Cys Tyr Ser
1 5 10 15
Leu Tyr Leu Glu Leu Glu Leu Gly Phe Arg Ser Leu Ser Gln Glu Val
20 25 30
Thr Arg Glu Trp Cys Leu Ser Tyr Phe Phe Leu Ile Lys Val Cys Trp
35 40 45
Gln Val Pro Val Ser Glu Phe Leu Leu Val Lys Glu Asn Pro Phe Leu
50 55 60
Leu Leu Glu Lys Lys Leu
65 70

<210> 170
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (80)
<223> Xaa equals stop translation

<400> 170
Met Pro Phe Ile Leu Leu Leu Val Cys Leu Thr Ser Leu Pro Ser Arg
1 5 10 15
Gly Tyr Asn Glu Lys Lys Leu Thr Asp Asn Ile Gln Cys Glu Ile Phe
20 25 30
Gln Val Leu Tyr Glu Glu Ala Thr Ala Ser Tyr Lys Glu Glu Ile Val
35 40 45
His Gln Leu Pro Ser Asn Lys Pro Glu Glu Leu Glu Asn Asn Val Asp
50 55 60
Gln Ile Leu Lys Trp Ile Glu Gln Trp Ile Lys Asp His Asn Ser Xaa
65 70 75 80

<210> 171

<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 171
Met Lys Ile Leu Ile Leu Phe Ile Phe Ile Pro Gly Leu Leu Val Glu
1 5 10 15

Lys Asn Gly Pro Asp His Val Cys Val Cys Met Cys Val Arg Val Cys
20 25 30

Val Cys Ala His Leu Gly Leu Phe Ile Xaa
35 40

<210> 172
<211> 131
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (66)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (94)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (102)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 172

Met Trp Ser Val Ile Arg Ser Leu Cys Pro Ser Arg Leu Gln Ser Leu
1 5 10 15

His Val Cys Phe Cys Pro Arg Leu Cys Leu Ala Val Pro Cys Val Phe
20 25 30

His Leu Ser Ser Pro Trp Phe His Val Arg Xaa Xaa Phe Phe Ser Gly
35 40 45

Xaa Pro Gly Cys Ile Trp Gly Ile Cys Phe Val Gly Leu Leu Leu Gly
50 55 60

Ala Xaa Arg Pro Arg Ser Gly Cys Leu Cys Ser Pro Ser Xaa Cys Leu
65 70 75 80

Trp Ser Leu Val Val Cys Glu Ser Ile Cys Leu Pro Arg Xaa Gly Pro
85 90 95

Asn Gln Ala Pro Pro Xaa Pro Leu Phe Leu Ser Leu Asn Leu Pro Phe
100 105 110

Leu Phe Gln Pro Leu Gln Met Arg Trp Leu Ser Ala Val Gly Trp Arg
115 120 125

Glu Ala Met
130

<210> 173

<211> 45

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (45)

<223> Xaa equals stop translation

<400> 173

Met Gln Leu Ser Leu Ser Leu Cys Ala Phe Val Val Cys Thr Asn Ala
1 5 10 15

Val Cys Thr His Ala Ala Thr Asn Gln Ala Arg Leu Val Gly Phe Leu
20 25 30

Lys Val Leu Arg Pro Ala His Ser Pro Leu Cys Leu Xaa
35 40 45

<210> 174

<211> 63

<212> PRT

<213> Homo sapiens

<220>

<221> SITE
 <222> (10)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (25)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (38)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (63)
 <223> Xaa equals stop translation

<400> 174
 Met Gln Pro Ala Trp Leu Trp Leu Trp Xaa Trp Glu Leu Gly Trp Glu
 1 5 10 15
 Leu Val Phe Gly Ala Ile Leu Leu Xaa Leu Gln Asp Gly Leu Phe Asp
 20 25 30
 Ser Val Leu Tyr Cys Xaa His Leu Tyr Ser Gly Leu Phe Phe Pro Trp
 35 40 45
 Ile Val Asn Ser Leu Met Ser Gly Ser Ser Gln Leu Met Ser Xaa
 50 55 60

<210> 175
 <211> 20
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (20)
 <223> Xaa equals stop translation

<400> 175
 Met Ser Ser Pro Lys Ser Leu Val Leu Leu Leu Ala Val Ile Cys Arg
 1 5 10 15
 Glu Ala Thr Xaa
 20

<210> 176
 <211> 41
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE

<222> (41)

<223> Xaa equals stop translation

<400> 176

Met Asn Ile Val Pro Gln Phe Ser Val Leu Pro His Phe Ala Tyr Phe
1 5 10 15

Ser Phe Ile Ile Leu Tyr Trp Ala Val Leu Phe Ser Gln Thr Ile Cys
20 25 30

Ser Met Ser Val Phe Lys Val Lys Xaa
35 40

<210> 177

<211> 49

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (49)

<223> Xaa equals stop translation

<400> 177

Met Thr Asp Ile Thr Cys Phe Leu Phe Ser Tyr Leu Ser Thr Leu Leu
1 5 10 15

Ser Pro Ile Tyr Leu Asp Val Leu Leu Phe Ser Leu Leu Leu Phe Leu
20 25 30

Phe His Ile Ala Gly Met His Ile Leu Thr Phe Ile Asn His Asp Ile
35 40 45

Xaa

<210> 178

<211> 107

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (59)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (63)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (65)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (77)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (88)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (107)
<223> Xaa equals stop translation

<400> 178
Met Gly Ala Ala Leu Ala Ala Trp Ile Cys Ile Val Arg Tyr His Gln
1 5 10 15
Leu Arg Asp Trp Gly Val Arg Arg Trp Pro Asn Gln Leu Ile Leu Trp
20 25 30
Thr Gly Leu Leu Cys Ala Leu Gly Thr Ser Val Val Gly Asn Leu Pro
35 40 45
Gly Glu Thr Gln Ser Ala Pro Arg Val Cys Xaa Arg Pro Ala Xaa Gly
50 55 60
Xaa Thr Thr Pro Ser Met Pro Arg Gly His Arg Leu Xaa Val Ser Gly
65 70 75 80
Ala Gly Ser Arg Pro Pro Phe Xaa Gly Leu Val Phe Phe Ser Gly His
85 90 95
Trp Pro Gly Pro Ala Gly Ser Phe Xaa Leu Xaa
100 105

<210> 179
<211> 46
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (46)
<223> Xaa equals stop translation

<400> 179
Met Gly Cys Trp Val Leu Phe Ile Leu Leu Tyr Leu Ala Leu His Ile
1 5 10 15
Cys Val Gln Asn Tyr Ile Tyr Ser Tyr Lys Ile Ile Cys Leu Gln Ser

20

25

30

Phe His Tyr Ile Val Arg Lys Ile Gln Ile Phe Val Ser Xaa
 35 40 45

<210> 180

<211> 67

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (67)

<223> Xaa equals stop translation

<400> 180

Met Leu Leu Ala Ala Phe Leu Ala Leu Phe Pro Leu His Asp Ser Arg
 1 5 10 15

Gly Leu Lys His Thr Gly Ala Gly His Val Asn Ser Val Ala Leu Leu
 20 25 30

Pro Ile Pro Leu Lys Ala Val Ser Leu Ser Pro Val Ser Ser Leu Gln
 35 40 45

Val Pro Cys Cys Cys Ser Ser Phe Gln Leu Leu Leu Thr Phe Leu Ser
 50 55 60

Val Ser Xaa
 65

<210> 181

<211> 50

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (50)

<223> Xaa equals stop translation

<400> 181

Met Ile Cys Lys Phe Leu Ile Ile Ile Cys Ile Thr Leu Leu Leu Phe
 1 5 10 15

Ala Ile Cys Gln Leu Cys Lys Arg Gln Gly Leu Val Gln Lys Ile Ser
 20 25 30

Phe Tyr Gln Lys Glu Thr Leu Ser Ser Thr Val Gly Thr Thr Phe Leu
 35 40 45

Ser Xaa
 50

<210> 182

<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (73)
<223> Xaa equals stop translation

<400> 182
Met Leu Thr Trp Val Trp Tyr Leu Ile Met Thr Ser Val Leu Gln Ala
1 5 10 15
Ser Val Ser Ser Val Val Arg Gly Ser Ile Leu Val Gly Gly Ser Glu
20 25 30
Asp Cys Xaa Glu Gly Gly Ser Leu Ile Gln Val Ser Leu Gly Tyr Val
35 40 45
Leu Ala Ala Arg Glu Asp Arg Gln Glu Cys Gly Pro Asp Thr Val Ser
50 55 60
Cys Pro Pro Gly Met Arg Leu Asp Xaa
65 70

<210> 183
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 183
Met Leu Ser Ala Leu Ser Ala Leu Tyr Leu Ile Ile Thr Ile Phe Leu
1 5 10 15
Lys Gly Ser Cys Cys Ser Cys His His Cys Phe Thr Asn Gly Lys Leu
20 25 30
Trp Leu Arg Lys Phe Ile Ser Gly Ser Gln Pro Xaa
35 40

<210> 184
<211> 58
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
 <222> (58)
 <223> Xaa equals stop translation

<400> 184

Met Cys Met Thr Val Phe Ile Val Phe Tyr Tyr Ser Phe Met Arg Leu
 1 5 10 15

Leu Phe Arg Cys Ser His Asn Arg Arg His Trp Arg Gly Ser Gly Lys
 20 25 30

Asn Thr Val Tyr His Thr Gly Pro Arg Asp Glu Ala Cys Cys Ala Met
 35 40 45

Pro Cys Trp Ala Thr Trp Gly Arg Arg Xaa
 50 55

<210> 185
 <211> 69
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (69)
 <223> Xaa equals stop translation

<400> 185

Met Pro Leu Ala Leu Lys Arg Gly Gln Leu Phe Leu Ile Pro Trp Leu
 1 5 10 15

Phe Pro Gln Gly Val Cys Pro Leu Glu Gly Glu Gln Leu Gly Ser Gly
 20 25 30

Lys Glu Gly Leu Leu Gln Phe Ala Ile Ala Ser Cys Pro Arg Val Tyr
 35 40 45

Pro Glu His Ser Pro Pro Trp Lys Glu Thr Gln Ser Ala Thr Gly Tyr
 50 55 60

Arg Lys Ser Asp Xaa
 65

<210> 186
 <211> 25
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (25)
 <223> Xaa equals stop translation

<400> 186

Met Lys Tyr Leu Leu Phe Leu Val Phe Cys Leu Ser Tyr Val Lys Asp
 1 5 10 15

Leu Asn Ile Phe Asp Leu Leu Tyr Xaa
20 25

<210> 187
<211> 58
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (58)
<223> Xaa equals stop translation

<400> 187
Met Thr Leu Pro Trp Glu Trp Val Pro Asp Lys Arg Ile Trp Leu Leu
1 5 10 15
Ser Leu Thr Leu Val His Ala Leu Leu Pro Leu Cys Leu Leu Pro Trp
20 25 30
Asp Val Gly Ala Arg Ser Pro Phe Ile Ser Gly Glu Pro Ile Asn Leu
35 40 45

Gly Phe Pro Asn Leu Gln Asn Cys Lys Xaa
50 55

<210> 188
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (67)
<223> Xaa equals stop translation

<400> 188
Met Val Gly Leu Leu Leu Ile Ala Leu Leu Thr Trp Gly Tyr Ile Arg
1 5 10 15
Tyr Ser Gly Gln Tyr Arg Glu Leu Gly Gly Ala Ile Asp Phe Gly Ala
20 25 30
Ala Tyr Val Leu Glu Gln Ala Ser Ser His Ile Gly Asn Ser Thr Gln
35 40 45
Ala Thr Val Arg Asp Ala Val Val Gly Arg Pro Ser Met Asp Lys Lys
50 55 60

Ala Gln Xaa
65

<210> 189
<211> 89

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (63)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (89)
<223> Xaa equals stop translation

<400> 189
Met Ser Thr Tyr Leu Lys Met Phe Ala Ala Ser Leu Leu Ala Met Cys
1 5 10 15

Ala Xaa Ala Glu Val Val His Arg Tyr Tyr Arg Pro Asp Leu Met Arg
20 25 30

Asn Arg Leu Arg Arg Val Lys Leu Ile Ser Gln Ser His Ile Ala Leu
35 40 45

Val Arg Arg Phe Glu Asp Leu Lys Pro Lys Leu Ser Val Cys Xaa Thr
50 55 60

Gly Ile Thr Ser Leu Ser Val Gly Glu Leu Glu Val Trp Ala Glu Ser
65 70 75 80

Ser Arg Gly Asp Leu Met Thr Ala Xaa
85

<210> 190
<211> 221
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (159)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (221)
<223> Xaa equals stop translation

<400> 190
Met Lys Leu Leu Leu Trp Ala Cys Ile Val Cys Val Ala Phe Ala Arg
1 5 10 15

Lys Arg Arg Phe Pro Phe Ile Gly Glu Asp Asp Asn Asp Asp Gly His

20

25

30

Pro Leu His Pro Ser Leu Asn Ile Pro Tyr Gly Ile Arg Asn Leu Pro
35 40 45

Pro Pro Leu Tyr Tyr Arg Pro Val Asn Thr Val Pro Ser Tyr Pro Gly
50 55 60

Asn Thr Tyr Thr Asp Thr Gly Leu Pro Ser Tyr Pro Trp Ile Leu Thr
65 70 75 80

Ser Pro Gly Phe Pro Tyr Val Tyr His Ile Arg Gly Phe Pro Leu Ala
85 90 95

Thr Gln Leu Asn Val Pro Pro Leu Pro Pro Arg Gly Phe Pro Phe Val
100 105 110

Pro Pro Ser Arg Phe Phe Ser Ala Ala Ala Ala Pro Ala Ala Pro Pro
115 120 125

Ile Ala Ala Glu Pro Ala Ala Ala Ala Pro Leu Thr Ala Thr Pro Val
130 135 140

Ala Ala Glu Pro Ala Ala Arg Gly Pro Val Ala Ala Glu Pro Xaa Gly
145 150 155 160

Arg Gly His Leu Leu Glu Leu Glu Pro Ala Ala Glu Ala Pro Val Ala
165 170 175

Ala Glu Pro Ala Ala Glu Ala Pro Val Gly Val Glu Pro Ala Ala Glu
180 185 190

Glu Pro Ser Pro Ala Glu Pro Ala Thr Ala Lys Pro Ala Ala Pro Glu
195 200 205

Pro His Pro Ser Pro Ser Leu Glu Gln Ala Asn Gln Xaa
210 215 220

<210> 191

<211> 52

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (52)

<223> Xaa equals stop translation

<400> 191

Met Glu Arg Leu Val Leu Ser Leu Trp Ser Leu Thr Cys Arg Ala Ser
1 5 10 15

Pro Ala Asn Thr His Pro Arg Thr Thr Ser Arg Thr Arg Thr Leu Asp
20 25 30

Val Lys Thr Lys Cys Pro Val Glu Ala Val Lys Leu Ser Glu Met Leu
35 40 45

Pro Pro Val Xaa
50

<210> 192
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (72)
<223> Xaa equals stop translation

<400> 192
Met Val Gly Thr His Leu Ile Leu Phe Pro Phe Leu Leu Arg Thr Met
1 5 10 15
Val Ile Phe Leu Cys Leu Lys Ser Ser Cys Gly Ser Phe Leu Pro Ile
20 25 30
Asn Lys Ile Gln Thr Pro Phe Ile Leu Asn Leu Ile Tyr Lys Thr Phe
35 40 45
Lys Met Cys Ser Leu Pro Asn Ser Leu Phe Ser Pro Leu Ser Phe Ile
50 55 60
Phe Phe Ile Phe Phe Leu Thr Xaa
65 70

<210> 193
<211> 112
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (108)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (112)
<223> Xaa equals stop translation

<400> 193
Met Arg Arg Leu Leu Leu Ala Leu Pro Phe Ala Leu Leu Pro Leu Ala
1 5 10 15
Val Ala His Ala His Glu Asp His Asp His Glu His Gly Ser Leu Gly
20 25 30
Ala His Glu His Gly Val Gly Arg Leu Asn Ala Val Leu Asp Gly Gln
35 40 45
Ala Leu Glu Leu Glu Leu Asp Ser Pro Ala Met Asn Leu Val Gly Phe

50

55

60

Glu His Val Ala Thr Ser Ala Ala Asp Lys Ala Lys Val Ala Ala Val
65 70 75 80

Arg Lys Gln Leu Glu Asn Pro Ser Gly Pro Val Gln Pro Ala Gln Ser
85 90 95

Arg Ser Cys Val Val Ser Asn Gln Gly Ile Asn Xaa Arg Cys Ser Xaa
100 105 110

<210> 194

<211> 61

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (14)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (61)

<223> Xaa equals stop translation

<400> 194

Met Phe Ile Thr Arg Gly Cys Tyr Cys Phe Val Phe Phe Xaa Leu Ala
1 5 10 15

His Asn Cys Lys Ala Ala Arg Thr Thr Arg Asn Gly Phe Pro Thr Val
20 25 30

Pro Gly Arg Arg Gln Arg Thr Leu Arg Arg Leu Phe Leu Cys Gly Phe
35 40 45

Pro Leu Leu Cys Ser Gln Gly Asp Leu Ser Ala Ala Xaa
50 55 60

<210> 195

<211> 126

<212> PRT

<213> Homo sapiens

<400> 195

Met Thr Lys Leu Ala Gln Trp Leu Trp Gly Leu Ala Ile Leu Gly Ser
1 5 10 15

Thr Trp Val Ala Leu Thr Thr Gly Ala Leu Gly Leu Glu Leu Pro Leu
20 25 30

Ser Cys Gln Glu Val Leu Trp Pro Leu Pro Ala Tyr Leu Leu Val Ser
35 40 45

Ala Gly Cys Tyr Ala Leu Gly Thr Val Gly Tyr Arg Val Ala Thr Phe
 50 55 60

His Asp Cys Glu Asp Ala Ala Arg Glu Leu Gln Ser Gln Ile Gln Glu
 65 70 75 80

Ala Arg Ala Asp Leu Ala Arg Arg Gly Cys Ala Ser Asp Ser Leu Thr
 85 90 95

Pro Phe Leu Cys Gly Gln Pro Phe Leu Pro Phe Pro Ile Lys Glu Pro
 100 105 110

Val Tyr Phe Leu Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
 115 120 125

<210> 196

<211> 113

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (109)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (113)

<223> Xaa equals stop translation

<400> 196

Met Ala Ala Leu Leu Leu Leu Pro Trp Leu Met Leu Leu Thr Gly Arg
 1 5 10 15

Val Ser Leu Ala Gln Phe Ala Leu Ala Phe Val Thr Asp Thr Cys Val
 20 25 30

Ala Gly Ala Leu Leu Cys Gly Ala Xaa Leu Leu Phe His Gly Met Leu
 35 40 45

Leu Leu Arg Gly Gln Thr Thr Trp Glu Trp Ala Arg Gly Gln His Ser
 50 55 60

Tyr Asp Leu Gly Pro Cys His Asn Leu Gln Ala Ala Leu Gly Pro Arg
 65 70 75 80

Trp Ala Leu Val Trp Leu Trp Pro Phe Leu Ala Ser Pro Leu Pro Gly
 85 90 95

Asp Gly Ile Thr Phe Gln Thr Thr Ala Asp Val Gly Xaa Thr Ala Ser
 100 105 110

Xaa

<210> 197
<211> 66
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (66)
<223> Xaa equals stop translation

<400> 197
Met Leu Gly Ile Thr Arg Leu Trp Val Leu Leu Lys Pro Cys Phe Pro
1 5 10 15
Arg Cys Tyr Ser Ser Thr Gly Gly Glu Val Leu Pro Arg Cys Cys Glu
20 25 30
Val Glu Ala Glu Val Gln Val Pro His Ser Ala Pro Met Asp Ser Arg
35 40 45
Glu Gly Gly Thr Val Pro Tyr Phe Gly Gly Cys Gly Ser Pro Arg Phe
50 55 60

Tyr Xaa
65

<210> 198
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (23)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 198
Met Ala Gln His His Leu Leu Ser Ile Leu Leu Ala Ile Leu Ser Cys
1 5 10 15
Ser Ser Gln Pro Arg Gln Xaa Arg Gly Ser Gly Ala Leu Pro Cys Glu
20 25 30
Val Cys Ser Ala Val Leu Leu Thr Cys Leu Arg Lys Ile Ser Gly Ser
35 40 45
Leu Cys Val Xaa

50

<210> 199
<211> 59
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals stop translation

<400> 199
Met Ile Gly Lys Ser Leu Val Met Phe Cys Phe Leu Ser Trp Gly Ala
1 5 10 15
Gly Val His Gly Cys Ala Leu Tyr Tyr Asn Ala Ser Asn Arg Ile Gly
20 25 30
Ile Phe Tyr Ile Phe Cys Phe Thr Tyr Leu Arg Leu His Glu Cys Val
35 40 45
Met Leu Ser Asn Leu Arg Val Asn Glu Leu Xaa
50 55

<210> 200
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 200
Met Leu Ser Pro Leu Ser Gln Ser Leu Leu Val Ala Leu Asn Val Leu
1 5 10 15
Phe Leu Leu Pro Asn Phe Leu Ala Leu Ser Lys Asn Leu Thr Tyr Asp
20 25 30
Cys Tyr Phe Arg Phe Phe Pro Thr Phe Phe Leu Pro Pro Lys Glu Met
35 40 45
Trp Tyr Leu Xaa
50

<210> 201
<211> 81
<212> PRT
<213> Homo sapiens

<220>
<221> SITE

<222> (81)

<223> Xaa equals stop translation

<400> 201

Met Cys Pro Ala Ala Ala Leu Ala Trp Pro Thr Ser Ala Ile Ser Leu
1 5 10 15

Ile Val Ser Leu Ala Pro Ser Trp Ala Ala Ala Arg Asp Asn Trp Ala
20 25 30

Ala Ser Pro Tyr Thr Thr Gln Ala Arg Pro Ala Leu Arg Ala Ala Leu
35 40 45

Thr Thr Ile Ser Gly Pro Met Pro Ala Ala Ser Pro Met Val Met Pro
50 55 60

Thr Gly Arg Glu Gly Phe Thr Val Leu Gly Met Gly Leu Arg Cys Gly
65 70 75 80

Xaa

<210> 202

<211> 70

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (70)

<223> Xaa equals stop translation

<400> 202

Met Phe Leu Ile Val Phe Cys Phe Leu Gln Ser Leu Ser Ala Met Pro
1 5 10 15

Ile Val Leu Ile Phe Tyr Arg Ser Ser Leu Lys Ile Leu Asn Arg Gly
20 25 30

Ile Gly Ser Gly Gln Ser Glu Trp Leu Glu Phe Trp Leu Ser Lys Lys
35 40 45

Asn Phe Ile Leu His Lys His Val Val Arg Ser Phe Cys Ala Tyr Ala
50 55 60

Ala Trp Ile Gly Cys Xaa
65 70

<210> 203

<211> 46

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (46)

<223> Xaa equals stop translation

<400> 203

Met Leu Leu Cys Ser Val Arg Asn Ile Leu Trp His Thr Ala Phe Leu
1 5 10 15

Gly Ser Ala Val Leu Cys Phe Val Leu Val Leu Val Leu His Leu Glu
20 25 30

Cys Leu Ile Ile Asp Ala Tyr Phe Asn Ser Ile Ser Phe Xaa
35 40 45

<210> 204

<211> 53

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (53)

<223> Xaa equals stop translation

<400> 204

Met Gly Thr Glu Ala Ser Pro Lys Arg Tyr Phe Phe Val Val Val Val
1 5 10 15

Val Leu Gly Ile Ile Val Pro Ile Leu Arg Ala Phe Pro Pro Pro Val
20 25 30

Pro Thr His Pro Asn Lys Met Trp Trp Cys Cys Leu Gln Lys Arg Glu
35 40 45

Val Leu Cys His Xaa
50

<210> 205

<211> 62

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (62)

<223> Xaa equals stop translation

<400> 205

Met Phe Cys Trp Ile Leu Val Cys Leu Ala Tyr Leu Lys Val Pro Leu
1 5 10 15

Leu Phe Phe Phe Phe Phe Phe Leu Ser Ala Leu Phe Cys Arg Thr Cys
20 25 30

Ser Asn Met Glu Asn Lys Ser Arg Arg Leu Ser Ser Asp Cys Tyr Leu
35 40 45

Cys Pro Lys Pro Pro Gln Thr Phe Met Leu Met Phe Tyr Xaa

50

55

60

<210> 206
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 206
Met Leu Phe Leu His Thr Arg Leu His Phe Pro Arg Tyr Thr Leu Leu
1 5 10 15
Ile Cys Lys Val Leu Leu Val Val Ala Ala Ser Val His Arg Pro Trp
20 25 30
Leu Arg Ser Ile Thr Gly Cys Phe Phe Thr Lys Xaa
35 40

<210> 207
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation

<400> 207
Met Ser Ala Ser Leu Cys Leu Phe Thr Gln Val Leu Lys Gly Ile Val
1 5 10 15
Trp Leu Pro Ile Leu Met Phe His Val Gly Ala Thr Lys Thr Ser Gly
20 25 30
Phe Ser Val Glu Gln Leu Tyr Ser Xaa
35 40

<210> 208
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (57)
<223> Xaa equals stop translation

<400> 208
Met Phe Lys Arg Met Cys Phe Phe Phe Gln Val Phe Leu Pro Leu Ala
1 5 10 15

Cys Thr Glu Leu Leu Trp Lys Gly Ala Pro Cys Arg His Ile Phe Gln
 20 25 30

Thr Gly Pro Asp Leu Leu Val Thr Gln Arg Cys Val His Ser Leu Leu
 35 40 45

Leu Gly Tyr Leu Ile Ser Ile Phe Xaa
 50 55

<210> 209
 <211> 126
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (126)
 <223> Xaa equals stop translation

<400> 209
 Met Met Thr Gln Thr Cys Ile Ile Leu Leu Ile His Thr Met Gln Val
 1 5 10 15

Cys Thr Thr His Pro Thr Val Leu Ser His Thr Leu Leu Gln Arg Pro
 20 25 30

Lys Pro Thr Asp Leu Phe Pro Lys Ala Thr Pro Thr Thr Ala Pro Met
 35 40 45

Pro Leu Arg Met Arg Pro Pro Gln Cys Leu Pro His Met Phe His Leu
 50 55 60

Gln Ser Arg Arg Phe Asp Gln Glu Ile Gly Leu Gln Gln Lys Ser Met
 65 70 75 80

Thr Gly Ile Leu Gln Thr Glu Lys Trp Thr Gln Glu Asn Phe Gly Leu
 85 90 95

Ser Gln Gly Val Phe Leu Asn Met Asn Leu Ala Ser His Gln Phe Phe
 100 105 110

Ser Met Lys Asp Gln Leu Pro Ser Leu Lys Leu Pro Asp Xaa
 115 120 125

<210> 210
 <211> 26
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (26)
 <223> Xaa equals stop translation

<400> 210

Met Val Asn Ile Phe Gly Phe Val Ser Cys Ile Val Phe Val Val Ala
1 5 10 15

Val Gln Leu Cys Tyr Met Lys Gln Pro Xaa
20 25

<210> 211
<211> 48
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation

<400> 211
Met Leu Gln Phe Leu Leu Gly Phe Thr Leu Gly Asn Val Val Gly Met
1 5 10 15

Tyr Leu Ala Gln Asn Tyr Asp Ile Pro Asn Leu Ala Lys Lys Leu Glu
20 25 30

Glu Ile Lys Lys Asp Leu Asp Ala Lys Lys Lys Pro Pro Ser Ala Xaa
35 40 45

<210> 212
<211> 45
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (45)
<223> Xaa equals stop translation

<400> 212
Met Ala Ser Gly Ser Trp Thr Ser Ala Pro Gly Ile Gly Val Ile Leu
1 5 10 15

Val Met Thr Val Cys Leu Ser His Cys Tyr Thr His Glu Trp Gly Leu
20 25 30

Trp Gly Gly Gly Gly Thr Gln Gly Leu Thr Asp Ser Xaa
35 40 45

<210> 213
<211> 52
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 213

Met Tyr Ile Leu Cys Ser Gly Leu Leu Gln Gly Gln Leu His Tyr Phe
1 5 10 15

Leu Gly Trp Ala Phe Leu Trp Leu Lys Leu Gly Cys Pro Trp Leu Ser
20 25 30

Gln Gly Ser Gln Pro Lys Arg His Ser Gly Glu Asn Leu Trp Pro Ile
35 40 45

Arg Glu Glu Xaa
50

<210> 214
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 214

Met Tyr Ser Leu Val Leu Thr Phe Leu Val Ser Phe Cys Ala Leu Ser
1 5 10 15

Lys Thr Phe Leu Asp His Trp Phe Gln Met Phe Ile Tyr Tyr Ile Leu
20 25 30

Phe Lys Asp Ser Glu Ile Gly Phe Cys His Pro Leu Leu Tyr Val Leu
35 40 45

Phe His Xaa
50

<210> 215
<211> 210
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (143)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
 <222> (179)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (182)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (210)
 <223> Xaa equals stop translation

<400> 215

Met Arg Ser Thr Ile Leu Leu Phe Cys Leu Leu Gly Ser Thr Arg Ser
 1 5 10 15

Leu Pro Gln Leu Lys Pro Ala Leu Gly Leu Pro Pro Thr Lys Leu Ala
 20 25 30

Pro Asp Gln Gly Thr Leu Pro Asn Gln Gln Gln Ser Asn Gln Val Phe
 35 40 45

Pro Ser Leu Ser Leu Ile Pro Leu Thr Gln Met Leu Thr Leu Gly Pro
 50 55 60

Asp Leu His Leu Leu Asn Pro Ala Ala Gly Met Thr Pro Gly Thr Gln
 65 70 75 80

Thr His Pro Leu Thr Leu Gly Gly Leu Asn Val Gln Gln Gln Leu His
 85 90 95

Pro His Val Leu Pro Ile Phe Val Thr Gln Leu Gly Ala Gln Gly Thr
 100 105 110

Ile Leu Ser Ser Glu Glu Leu Pro Gln Ile Phe Thr Ser Leu Ile Ile
 115 120 125

His Ser Leu Phe Pro Gly Xaa Ile Leu Pro Thr Ser Gln Ala Xaa Ala
 130 135 140

Asn Pro Asp Val Gln Asp Gly Ser Leu Pro Ala Gly Gly Ala Gly Val
 145 150 155 160

Asn Pro Ala Thr Gln Gly Thr Pro Ala Gly Arg Leu Pro Thr Pro Ser
 165 170 175

Gly Thr Xaa Asp Asp Xaa Ala Val Thr Thr Pro Ala Gly Ile Gln Arg
 180 185 190

Ser Thr His Ala Ile Glu Glu Ala Thr Thr Glu Ser Ala Asn Gly Ile
 195 200 205

Gln Xaa
 210

<210> 216
 <211> 195
 <212> PRT
 <213> Homo sapiens

<400> 216
 Met Ala Pro Ala Ala Ser Arg Leu Arg Ala Glu Ala Gly Leu Gly Ala
 1 5 10 15
 Leu Pro Arg Arg Ala Leu Ala Gln Tyr Leu Leu Phe Leu Arg Leu Tyr
 20 25 30
 Pro Val Leu Thr Lys Ala Ala Thr Ser Gly Ile Leu Ser Ala Leu Gly
 35 40 45
 Asn Phe Leu Ala Gln Met Ile Glu Lys Lys Arg Lys Lys Glu Asn Ser
 50 55 60
 Arg Ser Leu Asp Val Gly Gly Pro Leu Arg Tyr Ala Val Tyr Gly Phe
 65 70 75 80
 Phe Phe Thr Gly Pro Leu Ser His Phe Phe Tyr Phe Phe Met Glu His
 85 90 95
 Trp Ile Pro Pro Glu Val Pro Leu Ala Gly Leu Arg Arg Leu Leu Leu
 100 105 110
 Asp Arg Leu Val Phe Ala Pro Ala Phe Leu Met Leu Phe Phe Leu Ile
 115 120 125
 Met Asn Phe Leu Glu Gly Lys Asp Ala Ser Ala Phe Ala Ala Lys Met
 130 135 140
 Arg Gly Gly Phe Trp Pro Ala Leu Arg Met Asn Trp Arg Val Trp Thr
 145 150 155 160
 Pro Leu Gln Phe Ile Asn Ile Asn Tyr Val Pro Leu Lys Phe Arg Val
 165 170 175
 Leu Phe Ala Asn Leu Ala Ala Leu Phe Trp Tyr Ala Tyr Leu Ala Ser
 180 185 190
 Leu Gly Lys
 195

<210> 217
 <211> 35
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (35)
 <223> Xaa equals stop translation

<400> 217
 Met Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Ile Trp

1

5

10

15

Ser Ser Ala His Gln Tyr Lys Cys Pro Cys Tyr Ser Arg Gln Ser Gln
20 25 30

Glu Lys Xaa
35

<210> 218

<211> 72

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals stop translation

<400> 218

Met Phe Pro Ser Cys Leu Pro Leu Leu Phe Asn Ala Lys Val Leu Ala
1 5 10 15

Lys Asp Ile Phe Leu Leu Leu Leu Cys Phe Ser Ile Leu Phe Cys Thr
20 25 30

Val Gly Trp Leu Ser Ala Pro Thr Leu Gly Thr Gly Pro Trp Leu Gly
35 40 45

His Phe Met Ala Gln Ser Leu Trp Gly Leu Lys Glu Gly Trp Ala Ala
50 55 60

Gln Ser Leu His Gly Ser Cys Xaa
65 70

<210> 219

<211> 53

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (53)

<223> Xaa equals stop translation

<400> 219

Met Ala Val Ser Leu Trp Pro Glu Gly Ser Gly Pro Leu Cys Ala Leu
1 5 10 15

Ser Leu Leu Thr Cys Cys Leu Val Leu Arg Pro Ala Ser Ser Ser Gly
20 25 30

Phe Leu Trp Ser Leu Glu Glu Thr Pro Ala Leu Gln Gly Leu Cys Glu
35 40 45

Ile Ala Gln Pro Xaa
50

<210> 220
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals stop translation

<400> 220
Met Val His Asn Cys Leu Leu Leu Leu Lys Phe Leu Leu Leu Phe Cys
1 5 10 15
Phe Pro Leu Ile Ser Tyr Gln Leu Met Asn Gly Ser Leu Gln Ser Leu
20 25 30
Gln Arg Leu Arg Met Ile Gln Asn Val Gln Cys Ile Val Leu Asn Lys
35 40 45
Gln Glu Ala Glu Phe Leu Met Gly Ile Ser Phe Gln Ile Tyr Asp Trp
50 55 60
Ser Leu Gly Phe Xaa
65

<210> 221
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals stop translation

<400> 221
Met Ser His Leu Gln Thr Leu His Leu Ile Gly Leu Ser Cys Ser Phe
1 5 10 15
Leu Tyr Phe Pro Thr Ser Gln Ala Val Glu Ala Ala Glu Pro Gly Met
20 25 30
Met Leu Ser Leu Arg Gln Met Thr Asn Pro Leu Val Ala Arg Asn Gln
35 40 45
Thr Ala Pro Arg Ala Gly Val Ser Val Phe Cys Thr Asp Cys Leu Phe
50 55 60
Gly Leu Asp Ile Xaa
65

<210> 222
<211> 44

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 222
Met Leu Thr Cys Ile Asp Met Asp Trp Lys Val Leu Thr Trp Leu Arg
1 5 10 15
Tyr Thr Leu Trp Ile Pro Leu Tyr Pro Leu Gly Met Phe Gly Gly Ser
20 25 30
Cys Leu Ser Asp Ser Val His Ser Asn Ile Gln Xaa
35 40

<210> 223
<211> 103
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (103)
<223> Xaa equals stop translation

<400> 223
Met Trp Ser Ser Ile Arg Leu Leu Ser Pro Val Leu Ser Leu Ile Leu
1 5 10 15
Leu Leu Ile Ala Leu Glu Leu Val Asn Ile His Ala Val Cys Gly Lys
20 25 30
Asn Ala His Glu Tyr Gln Gln Tyr Leu Lys Phe Val Lys Ser Ile Leu
35 40 45
Gln Tyr Thr Glu Asn Leu Val Ala Tyr Thr Ser Tyr Glu Lys Asn Lys
50 55 60
Trp Asn Glu Thr Ile Asn Leu Thr His Thr Ala Leu Leu Lys Met Trp
65 70 75 80
Thr Phe Ser Glu Lys Lys Gln Met Leu Ile His Leu Ala Lys Lys Ser
85 90 95
Thr Ser Lys Val Leu Leu Xaa
100

<210> 224
<211> 214
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (214)
<223> Xaa equals stop translation

<400> 224

Met Lys Gly Phe Ser Trp Ala Ile Val Pro Ala Leu Thr Ser Leu Gly
1 5 10 15

Tyr Leu Ile Ile Leu Val Val Ser Ile Phe Pro Phe Trp Val Arg Leu
20 25 30

Thr Asn Glu Glu Ser His Glu Val Phe Phe Ser Gly Leu Phe Glu Asn
35 40 45

Cys Phe Asn Ala Lys Cys Trp Lys Pro Arg Pro Leu Ser Ile Tyr Ile
50 55 60

Ile Leu Gly Arg Val Phe Leu Leu Ser Ala Val Phe Leu Ala Phe Val
65 70 75 80

Thr Thr Phe Ile Met Met Pro Phe Ala Ser Glu Phe Phe Pro Arg Thr
85 90 95

Trp Lys Gln Asn Phe Val Leu Ala Cys Ile Ser Phe Phe Thr Gly Ala
100 105 110

Cys Ala Phe Leu Ala Leu Val Leu His Ala Leu Glu Ile Lys Ala Leu
115 120 125

Arg Met Lys Leu Gly Pro Leu Gln Phe Ser Val Leu Trp Pro Tyr Tyr
130 135 140

Val Leu Gly Phe Gly Ile Phe Leu Phe Ile Val Ala Gly Thr Ile Cys
145 150 155 160

Leu Ile Gln Glu Met Val Cys Pro Cys Trp His Leu Leu Ser Thr Ser
165 170 175

Gln Ser Met Glu Glu Asp His Gly Ser Leu Tyr Leu Asp Asn Leu Glu
180 185 190

Ser Leu Gly Gly Glu Pro Ser Ser Val Gln Lys Glu Thr Gln Val Thr
195 200 205

Ala Glu Thr Val Ile Xaa
210

<210> 225
<211> 109
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (34)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (48)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (109)

<223> Xaa equals stop translation

<400> 225

Met	Thr	Val	Ser	Gly	Thr	Val	Val	Leu	Val	Ala	Gly	Thr	Leu	Cys	Phe
1				5				10						15	

Ala	Trp	Trp	Ser	Glu	Gly	Asp	Ala	Thr	Ala	Gln	Pro	Gly	Gln	Leu	Ala
			20					25					30		

Pro	Xaa	Thr	Glu	Tyr	Pro	Val	Pro	Glu	Gly	Pro	Ser	Pro	Leu	Leu	Xaa
		35				40					45				

Ser	Val	Ser	Phe	Val	Cys	Cys	Gly	Ala	Gly	Gly	Leu	Leu	Leu	Leu	Ile
	50				55						60				

Gly	Leu	Leu	Trp	Ser	Val	Lys	Ala	Ser	Ile	Pro	Gly	Pro	Pro	Ser	Met
65					70					75					80

Gly	Pro	Leu	Ser	Pro	Leu	Gln	Arg	Pro	Val	Leu	Pro	His	Cys	Gly	Val
				85					90					95	

Leu	Arg	Glu	Gly	Glu	Leu	Gln	Asp	Pro	Gln	Ser	Gly	Xaa
				100				105				

<210> 226

<211> 316

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (316)

<223> Xaa equals stop translation

<400> 226

Met	Glu	Ser	Leu	Tyr	Asp	Leu	Trp	Glu	Phe	Tyr	Leu	Pro	Tyr	Leu	Tyr
1				5				10					15		

Ser	Cys	Ile	Ser	Leu	Met	Gly	Cys	Leu	Leu	Leu	Leu	Cys	Thr	Pro
			20					25				30		

Val	Gly	Leu	Ser	Arg	Met	Phe	Thr	Val	Met	Gly	Gln	Leu	Leu	Val	Lys
		35					40					45			

Pro	Thr	Ile	Leu	Glu	Asp	Leu	Asp	Glu	Gln	Ile	Tyr	Ile	Ile	Thr	Leu
	50					55					60				

Glu	Glu	Glu	Ala	Leu	Gln	Arg	Arg	Leu	Asn	Gly	Leu	Ser	Ser	Ser	Val
65					70					75					80

Glu	Tyr	Asn	Ile	Met	Glu	Leu	Glu	Gln	Glu	Leu	Glu	Asn	Val	Lys	Thr	
				85					90						95	
Leu	Lys	Thr	Lys	Leu	Asp	Pro	Trp	Ser	Ser	Phe	Ser	Val	Leu	Gln	Ser	
			100					105					110			
Pro	Val	Trp	His	Phe	Ala	Ala	Gln	Thr	Pro	Ala	Asp	Ile	Val	Ser	Pro	
		115					120					125				
Asp	Ser	His	Phe	Met	Leu	Ser	Thr	Gln	Gly	Met	Ser	Trp	Ala	Gln	Leu	
	130					135					140					
Val	Phe	Leu	Leu	Pro	Ala	Ser	Arg	Pro	Gly	Asn	Ser	Gln	Asp	Lys	Arg	
145					150					155					160	
Arg	Lys	Lys	Ala	Ser	Ala	Trp	Glu	Arg	Asn	Leu	Val	Tyr	Pro	Ala	Val	
				165					170					175		
Met	Val	Leu	Leu	Leu	Ile	Glu	Thr	Ser	Ile	Ser	Val	Leu	Leu	Val	Ala	
			180					185					190			
Cys	Asn	Ile	Leu	Cys	Leu	Leu	Val	Asp	Glu	Thr	Ala	Met	Pro	Lys	Gly	
		195					200					205				
Thr	Arg	Gly	Pro	Gly	Ile	Gly	Asn	Ala	Ser	Leu	Ser	Thr	Phe	Gly	Phe	
	210					215						220				
Val	Gly	Ala	Ala	Leu	Glu	Ile	Ile	Leu	Ile	Phe	Tyr	Leu	Met	Val	Ser	
225					230					235					240	
Ser	Val	Val	Gly	Phe	Tyr	Ser	Leu	Arg	Phe	Phe	Gly	Asn	Phe	Thr	Pro	
				245					250					255		
Lys	Lys	Asp	Asp	Thr	Thr	Met	Thr	Lys	Ile	Ile	Gly	Asn	Cys	Val	Ser	
			260					265					270			
Ile	Leu	Val	Leu	Ser	Ser	Ala	Leu	Pro	Val	Met	Ser	Arg	Thr	Leu	Gly	
		275					280						285			
Leu	His	Lys	Leu	His	Leu	Pro	Asn	Thr	Ser	Arg	Asp	Ser	Glu	Thr	Ala	
	290					295					300					
Lys	Pro	Ser	Val	Asn	Gly	His	Gln	Lys	Ala	Leu	Xaa					
305					310					315						

Met Leu Ala Leu Ser Ser Phe Leu Val Leu Ser Tyr Leu Leu Thr
 1 5 10 15
 Arg Trp Cys Gly Ser Val Gly Phe Ile Leu Ala Asn Cys Phe Asn Met
 20 25 30
 Gly Ile Arg Ile Thr Gln Ser Leu Cys Phe Ile His Arg Tyr Tyr Arg
 35 40 45
 Arg Ala Pro Thr Gly Pro Trp Leu Ala Cys Thr Tyr Arg Gln Ser Cys
 50 55 60
 Ser Gly His Leu Pro Ser Val Val Gly Leu Leu Leu Phe Arg Arg Tyr
 65 70 75 80
 Ser Ser Ala Val Ser Arg Ala Gly Gln Pro Asp Trp His Thr Leu Leu
 85 90 95
 Trp Gly Pro Ser Val Trp Glu Gln Leu Ser Gly Gln His Ser Ser Gln
 100 105 110
 Arg Pro Ser Xaa
 115

<210> 228
 <211> 107
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (107)
 <223> Xaa equals stop translation

<400> 228
 Met Cys Val Gly Trp Trp Trp Trp Leu Val Val Leu Gly Leu Gly Met
 1 5 10 15
 Gly Gly Thr Leu Gly Cys Asp Gly Phe Leu Ser Gln Arg Trp Cys Phe
 20 25 30
 Thr Ala Gly Lys Tyr Leu Glu Leu Gly Gly Gly Leu Ser Arg His Gln
 35 40 45
 Ala Asp Phe Ile Phe Ser Gln Thr Lys Ala Thr Phe Thr Ser Lys Gly
 50 55 60
 Lys Thr Gln Asn Thr Lys Ile Glu Thr Ser Met Pro Pro His Leu Phe
 65 70 75 80
 Arg Gln Gln Glu Pro Pro Gly Gln Arg Val Phe Leu Thr Leu Arg Val
 85 90 95
 Thr Leu Thr Ser His Leu Val Ser Cys Gly Xaa
 100 105

<210> 229
<211> 38
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (38)
<223> Xaa equals stop translation

<400> 229
Met Ser Ser Phe Thr Leu Gly Leu Leu Phe Leu Phe Ile Phe Thr Thr
1 5 10 15
Ala Glu Asn Tyr Leu Ile Leu Phe Gln Arg Lys Tyr Cys Leu Val Ile
20 25 30
Phe Trp Gly Glu Phe Xaa
35

<210> 230
<211> 68
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (68)
<223> Xaa equals stop translation

<400> 230
Met Gln Thr Ser Gln Gln Leu Cys Cys Leu Ala Ile Ser Ile Leu Ala
1 5 10 15
Thr Leu Leu Pro Ser Gly Ala Ser Glu Glu Arg Ser Gly Leu Arg Pro
20 25 30
Gly Met Arg Leu Gln Glu Arg Glu Gln Arg Arg Ala Thr Phe Gly Ala
35 40 45
Ser Val His Ser Ser Phe Ile Ser Phe Cys Leu Leu His Gly Val Leu
50 55 60
Asn Lys Phe Xaa
65

<210> 231
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 231

Met Glu Leu Ser Leu Ala Val Leu Glu Ala Val Cys Gln Cys Leu Leu
1 5 10 15

Gly Leu Trp Leu Leu Phe Trp Leu Asp Lys Glu Val Ala Val Phe Val
20 25 30

Leu Leu Leu Trp Leu Phe Thr Asp Leu Thr Asp Val Thr Gly Asp Glu
35 40 45

Cys Arg Xaa
50

<210> 232

<211> 41

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Xaa equals stop translation

<400> 232

Met Lys Leu Leu Phe Cys Leu Arg Tyr Tyr Met Leu Leu Ser Val Val
1 5 10 15

Val Lys Ala Thr Ser Thr Ile Pro Ser Asn Ile Glu Ile Thr Ser Leu
20 25 30

Ser Trp Val Cys His Asn Ser Thr Xaa
35 40

<210> 233

<211> 42

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (42)

<223> Xaa equals stop translation

<400> 233

Met Arg Leu Val Ser Pro Gly Phe Trp Trp Val Leu Pro Leu Arg Leu
1 5 10 15

Gly Glu Ala Leu Pro Gly Arg Arg Arg Gln Gln Pro Pro Gly Ala Met
20 25 30

Lys Thr Leu Arg Leu Arg Glu Val Lys Xaa
35 40

<210> 234

<211> 48

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation

<400> 234
Met Trp Gly Pro Phe Cys Pro Phe Leu Phe Leu Phe Ser Arg Leu Ser
1 5 10 15
Asn Ser Leu Thr Lys Asp Ser Met Asn Ile Lys Ala His Ile His Met
20 25 30
Leu Leu Glu Val Arg Ala Ala His Pro Thr Thr Arg Leu Cys Val Xaa
35 40 45

<210> 235
<211> 40
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (40)
<223> Xaa equals stop translation

<400> 235
Met Phe Ile Leu Ala Ile Trp Asn Phe Phe Ile Leu Tyr Leu Phe Ser
1 5 10 15
Thr Val Ala Gly Leu Val Cys Lys Ser Leu Cys Gln Asn Gln Thr Ile
20 25 30
Phe Lys Thr Ala Leu Cys Phe Xaa
35 40

<210> 236
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (64)
<223> Xaa equals stop translation

<400> 236
Met Leu Arg Gly Trp Ala Leu Ser Thr Phe Leu Val Cys Ile Leu Gln
1 5 10 15
Trp Val Arg Ser Leu Thr Ile Arg Leu Ala Ser Ala Leu Ser Val Arg

20

25

30

Gly Pro Ser Ser Ile Pro Ala Ser Leu Ala Ile Ile Tyr Thr Leu Phe
35 40 45

Ile Phe Ser Phe Lys Phe Leu Lys Ile Val Lys Ser Ile Tyr Ile Xaa
50 55 60

<210> 237

<211> 61

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (61)

<223> Xaa equals stop translation

<400> 237

Met Arg Lys Val Thr Ile Ser Lys Lys His Ala Leu Leu Leu Cys Phe
1 5 10 15

Gln Leu Phe Arg Cys Leu Leu Ser Met Tyr Ile Trp Ile Thr Phe Val
20 25 30

Leu Asp Gly Ser Cys Gly Ile His Cys Ser Leu Lys Pro Val Ser Phe
35 40 45

Pro Cys Thr Tyr His Ser Val His Ser Ser Thr Ser Xaa
50 55 60

<210> 238

<211> 63

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (63)

<223> Xaa equals stop translation

<400> 238

Met Cys Ala Leu Gly Val Phe Leu Leu Val Pro Trp Tyr Glu Tyr Tyr
1 5 10 15

Leu Val Leu Leu Phe Phe Pro Cys Val Ala Phe Ser Val Val Ser Gly
20 25 30

Phe Phe Leu Cys Asn Asp Ser Lys Arg Thr Leu His Ser Cys Ala Leu
35 40 45

Cys Leu Cys Ala Gly Ile Cys Phe Pro Tyr Met Phe Leu Phe Xaa
50 55 60

<210> 239
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (45)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (57)
<223> Xaa equals stop translation

<400> 239
Met Met Leu His Xaa Lys Leu Leu Leu Phe Xaa Glu Ala Leu Trp Tyr
1 5 10 15
Tyr Gly Gly Gly Ala Phe Leu Cys Cys Ala Gly Ser Val Pro Thr Asp
20 25 30
Cys Tyr Phe Gly Gly Leu Asp Gln Arg Arg Leu Val Xaa Asp Lys Cys
35 40 45
Thr Glu Lys Ser Thr Gly Leu Leu Xaa
50 55

<210> 240
<211> 182
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (182)
<223> Xaa equals stop translation

<400> 240
Met Thr Val Ile Leu Ile Ile Leu Ile Val Val Met Ala Arg Tyr Cys
1 5 10 15
Arg Ser Lys Asn Lys Asn Gly Tyr Glu Ala Gly Lys Lys Asp His Glu
20 25 30

Asp Phe Phe Thr Pro Gln Gln His Asp Lys Ser Lys Lys Pro Lys Lys
 35 40 45
 Asp Lys Lys Asn Lys Lys Ser Lys Gln Pro Leu Tyr Ser Ser Ile Val
 50 55 60
 Thr Val Glu Ala Ser Lys Pro Asn Gly Gln Arg Tyr Asp Ser Val Asn
 65 70 75 80
 Glu Lys Leu Ser Asp Ser Pro Ser Met Gly Arg Tyr Arg Ser Val Asn
 85 90 95
 Gly Gly Pro Gly Ser Pro Asp Leu Ala Arg His Tyr Lys Ser Ser Ser
 100 105 110
 Pro Leu Pro Thr Val Gln Leu His Pro Gln Ser Pro Thr Ala Gly Lys
 115 120 125
 Lys His Gln Ala Val Gln Asp Leu Pro Pro Ala Asn Thr Phe Val Gly
 130 135 140
 Ala Gly Asp Asn Ile Ser Ile Gly Ser Asp His Cys Ser Glu Tyr Ser
 145 150 155 160
 Cys Gln Thr Asn Asn Lys Tyr Ser Lys Gln Met Arg Leu His Pro Tyr
 165 170 175
 Ile Thr Val Phe Gly Xaa
 180

<210> 241

<211> 71

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (71)

<223> Xaa equals stop translation

<400> 241

Met His Met Tyr Val Trp Val Arg Ala His Leu Val Phe Tyr Leu Phe
 1 5 10 15
 Val Cys Leu Ser Glu Ser Ser Ala Gly Gln Arg Leu Pro Leu Asp Cys
 20 25 30
 Cys Cys Ser Gly Asp Glu Lys Asp Glu Glu Ser Ala Gly Lys Arg Gly
 35 40 45
 Gly Val Gln Glu His Gly Gly His Leu Gly Pro Ser Phe Trp His Thr
 50 55 60
 Lys Pro Glu Phe Ser Cys Xaa
 65 70

<210> 242
<211> 62
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (62)
<223> Xaa equals stop translation

<400> 242
Met Trp Arg Val Met Leu Ala Trp Leu Ala Met Val Asn Ser Pro Met
1 5 10 15
Ala Met Glu Ser Gln Val Gly His Ile Ile Ala Val Lys Asp Thr Leu
20 25 30
Thr Gln Met Thr Leu Pro Gly Ala Arg Ile Glu Pro Val Arg Lys Glu
35 40 45
Ser Lys Ala Gly Ser Ala Gly Lys Arg Glu Gly Phe Cys Xaa
50 55 60

<210> 243
<211> 35
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals stop translation

<400> 243
Met Ile Ala Asp Trp Met Phe Phe Val Tyr Ala Leu Cys Ile Asp Val
1 5 10 15
Thr Ala Asn Glu Phe Cys Leu Thr Leu Thr Phe Leu Thr Ser Lys Val
20 25 30
Ser Lys Xaa
35

<210> 244
<211> 47
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (47)
<223> Xaa equals stop translation

<400> 244
Met Glu Pro Val Ala Leu Leu Gln Pro Thr Trp Trp Leu Leu Asn Val
1 5 10 15

Thr Leu Pro Leu Val Ala Trp Ser Gly Pro Leu Ile Cys Arg Pro Leu
20 25 30

Leu His Gly Glu Gly Arg Gln Gly Ala Ala Cys Leu Gln Gly Xaa
35 40 45

<210> 245

<211> 51

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (51)

<223> Xaa equals stop translation

<400> 245

Met His Phe Lys Arg Thr Gln Asn His Leu Asn Ile Val Thr Trp Leu
1 5 10 15

Leu Gln Val Met Ile Ile Val Met Leu Ile Ile Met Arg Ile Ser Cys
20 25 30

Thr His Gln Pro Val Glu Ser Lys Lys Phe Pro Phe Arg Asn Phe Leu
35 40 45

Ser Cys Xaa
50

<210> 246

<211> 51

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (51)

<223> Xaa equals stop translation

<400> 246

Met Thr Tyr His Val Val Cys Ala Phe Leu Ile Val Val Leu Lys Lys
1 5 10 15

Gln Phe Ile Leu Ala Leu Gln Thr Ile Ser Thr Ser Leu Arg Ser Lys
20 25 30

Gln Ile Leu Met Val Leu Ser Ser Thr Ile Ile Ala Asp Ser Thr Phe
35 40 45

Tyr Tyr Xaa
50

<210> 247

<211> 33

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (33)
<223> Xaa equals stop translation

<400> 247
Met Pro Val Pro Leu Trp Leu Val Leu Trp Phe Cys Phe Leu Leu Tyr
1 5 10 15
Val Ala Ser Arg Arg Thr Phe Gly Leu Ala Asn Tyr Met Pro Leu Pro
20 25 30

Xaa

<210> 248
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 248
Met Leu Ile Cys Arg Leu Val Leu Leu Ala Asp Pro Gly Pro Val Asn
1 5 10 15
Phe Met Val Arg Leu Phe Val Val Ile Val Met Phe Ala Trp Ser Ile
20 25 30
Val Gly Lys Tyr Val Leu Ile Ser Thr Ile Thr Glu Gln Thr Lys Thr
35 40 45

Xaa

<210> 249
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (116)
<223> Xaa equals stop translation

<400> 249
Met Ile Asn Val Tyr Phe Ser Gly Pro Gly Val Leu Thr Pro Leu Asp
1 5 10 15
Asp Gln Gly Ser Pro Cys Pro Pro Ala Pro Phe Ala Ala Leu His Pro

20

25

30

Cys Pro His Pro Ala Gly Ser Gly Val Leu Cys Cys Cys Pro Leu Arg
 35 40 45

Leu Cys Arg Pro Cys Arg Ile Leu Phe Thr Gly Pro Leu Leu Leu Thr
 50 55 60

Leu His His Leu Leu Cys Glu Thr Ser Pro Ser Gly Ile Gly Val Gly
 65 70 75 80

Asn Ile Val Pro Gly Ala Arg Pro Leu Gly Val Asn Pro Val Phe Pro
 85 90 95

Ile Ser Ser Cys Asp Leu Gly Gln Val Ala Glu Pro Leu Leu Val Thr
 100 105 110

Ile Ser Ser Xaa
 115

<210> 250

<211> 75

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (75)

<223> Xaa equals stop translation

<400> 250

Met Thr Asn Val Tyr Ser Leu Asp Gly Ile Leu Val Phe Gly Leu Leu
 1 5 10 15

Phe Val Cys Thr Cys Ala Tyr Phe Lys Lys Val Pro Arg Leu Lys Thr
 20 25 30

Trp Leu Leu Ser Glu Lys Lys Gly Val Trp Gly Val Phe Tyr Lys Ala
 35 40 45

Ala Val Ile Gly Thr Arg Leu His Ala Ala Val Ala Ile Ala Cys Val
 50 55 60

Val Met Ala Phe Tyr Val Leu Phe Ile Lys Xaa
 65 70 75

<210> 251

<211> 63

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (57)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (63)

<223> Xaa equals stop translation

<400> 251

Met Pro Thr Leu Arg Val Pro Val Leu Ser Val Trp Leu Leu Arg Trp
1 5 10 15

Trp Arg Val Leu Gly Ala Gly Arg Val Leu Pro Asp Ser Leu Ser Leu
20 25 30

Ser Pro Pro Pro Pro Thr Gly Cys Gln Thr Lys Pro Glu Arg Gly Trp
35 40 45

Gly Ser Gln Pro Pro Ser Val Leu Xaa Pro Gln Ala Pro Val Xaa
50 55 60

<310> 252

<311> 73

<312> PRT

<313> Homo sapiens

<220>

<221> SITE

<222> (73)

<223> Xaa equals stop translation

<400> 252

Met Val Tyr Tyr Leu Asn Arg Ala Leu Arg Ala Thr Phe Ser Ile Leu
1 5 10 15

Phe Ser Val Val Cys Leu Leu Phe Leu Gly Ser Ile Val Asn Cys Phe
20 25 30

Leu Asn Asp Val Phe Lys Pro Leu Thr Leu Asn Phe Ser Thr Ala Leu
35 40 45

Ser Ala Trp Arg Lys Glu Ser Ser Ala Trp Asn Ser Leu Gly Leu Leu
50 55 60

Pro Pro Thr Asp Glu Tyr Pro Thr Xaa
65 70

<310> 253

<311> 49

<312> PRT

<313> Homo sapiens

<220>

<221> SITE

<222> (49)

<223> Xaa equals stop translation

<400> 253

Met Val Val Asn Asp Arg Leu Val Ser Thr Cys Ile Leu Cys Thr Leu

1

5

10

15

His Ile Pro Leu Phe Phe Leu Ile Phe Leu Val Tyr Glu Val His Leu
20 25 30

Val Phe Gln Ile Val Ala Asn Leu Gln Lys Ile Phe Gln Tyr Ile Tyr
35 40 45

Xaa

<210> 254

<211> 41

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (41)

<223> Xaa equals stop translation

<400> 254

Met Ile Ile Leu His Ile Val Val Cys Leu Phe Thr Ile Ser Ile Ile
1 5 10 15

Glu Glu Gln Lys Glu Glu Ile Leu Cys Ser Thr Lys Ser Gln Ala Glu
20 25 30

Lys Thr Val Thr His Ile Glu Gln Xaa
35 40

<210> 255

<211> 54

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (54)

<223> Xaa equals stop translation

<400> 255

Met Thr Leu Ser Val Leu Phe Ala Phe Pro Ile Trp Leu Lys Tyr Leu
1 5 10 15

Asn Leu Asn Ile Phe Phe Leu Ala Leu Lys Ile Phe Trp Val Ile Leu
20 25 30

Ser Phe Cys Thr Ser Cys Thr Ser Trp Tyr Ser Gly Ala Arg Val Ile
35 40 45

Phe Phe Gln Ile Ile Xaa
50

<210> 256

<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation

<400> 256
Met Cys Arg Arg Ile Gln Arg Leu Arg Ala Met Leu His Met Leu Leu
1 5 10 15

Val Ser Met Leu Pro Thr Val Gly Lys Pro Asn Met Tyr Gln Pro Pro
20 25 30

Gln Asn Tyr Asp Ile Leu Leu Gln Xaa
35 40

<210> 257
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 257
Met Ala Leu Ala Phe Leu His Leu Asn Ile Ser Xaa Ser Gln Ala Leu
1 5 10 15

Thr Leu Cys Lys Glu Leu Glu Lys Pro Lys Leu Glu Lys Asn Lys Gly
20 25 30

Gly Pro Ala Leu Glu Lys Leu Val Val Xaa
35 40

<210> 258
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (53)
<223> Xaa equals stop translation

<400> 258
Met Ser Gly Thr Thr Trp Thr Ala Ile His Leu Thr Ser Asn Leu Phe

1 5 10 15
Gly Ile Leu Ala Leu Pro Gly Asn Gln Ser Ser Gly Ser Asn Ile Glu
20 25 30
Gln Leu Cys Thr Ser Ser Arg Glu Ala Thr Asn Arg Leu Pro Cys Val
35 40 45
Asp Val Gly Ser Xaa
50

<210> 259
<211> 48
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation

<400> 259
Met Phe Tyr Pro Pro Cys Pro Phe Phe Pro Gln Leu Cys Phe Cys Ile
1 5 10 15
Phe Phe Leu Gly Lys Cys Lys Leu Ser Leu Ser Phe Met Thr Cys Glu
20 25 30
Ile Ser Val Ser Leu Glu Phe Val Arg Arg Arg Gly Asn His Ala Xaa
35 40 45

<210> 260
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (53)
<223> Xaa equals stop translation

<400> 260
Met Asn Ser Trp Ile Leu Asn Met Arg Val Arg Phe Thr Phe Leu Ser
1 5 10 15
Gln Leu Leu Thr Leu Ile Pro Arg Thr Ser His Ser Ala Thr Ser Val
20 25 30
Gly Asn Ser Gln Ile Glu Leu Pro Arg Glu Lys His His Met Thr Tyr
35 40 45

Trp Glu Asn Gly Xaa
50

<210> 261
<211> 55
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> Xaa equals stop translation

<400> 261
Met Phe Ile Val Ile Cys Lys Ile Leu Leu Phe Leu Ile Leu Val Ala
1 5 10 15
Arg Pro Phe Arg Thr His Ser Cys Ile Lys Tyr Phe Ala Leu Phe Lys
20 25 30
Glu Thr His Met Asp Glu Val Arg Met Cys Asn Met Met Ala Ser Gln
35 40 45
Cys Ser Ser Leu Tyr Leu Xaa
50 55

<210> 262
<211> 38
<212> PRT
<213> Homo sapiens

<400> 262
Met Lys Asn Met Asn Ser Arg Tyr Tyr Leu Arg Ala Ile Phe Cys Leu
1 5 10 15
Tyr Thr Leu Ala Cys Ile Leu Phe Leu Gln Ile Ile Leu Lys Ala Arg
20 25 30
Cys Gly Gly Ser Arg Leu
35

<210> 263
<211> 24
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (24)
<223> Xaa equals stop translation

<400> 263
Met Pro Pro Leu Phe Leu Gly Ser Phe Leu Val Leu Trp Leu Gly Gly
1 5 10 15
Val Val Leu Cys Thr Gly Gly Xaa
20

<210> 264
<211> 47
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (47)
<223> Xaa equals stop translation

<400> 264
Met Val Cys Ala Leu Gly Val Tyr Val Cys Xaa Ser Ala Pro Thr Ala
1 5 10 15

Ala Val Pro Lys Pro Ala Lys Gly Thr Ile Cys Leu Lys Met Leu Ser
20 25 30

Gly Ala Asn Cys Ala Cys Gln Gly Gln Val Thr Arg Gln His Xaa
35 40 45

<210> 265
<211> 115
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (13)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals stop translation

<400> 265
Met Ala Gly Pro Arg Ala Ser Thr Gly Pro Arg Pro Xaa Cys Leu Val
1 5 10 15

Leu Phe Leu Phe Asn Phe Ile Phe Cys Phe Met Ser Val Cys Pro Pro
20 25 30

Thr Pro Thr Pro Phe Ser Val Lys Trp Gly Ala Leu Gly Glu Ser Leu
35 40 45

Leu Pro Pro Ser Leu Ser Gln Asp Leu Pro Pro Arg His Gln Pro Ser
50 55 60

Leu Trp Thr Arg Gln Arg Ala Asp Arg Val Gly Arg Gly Leu Arg Val
65 70 75 80

165

170

175

Ala Gly Gln Ala Gly Lys Glu Leu Gln Asn Ala His Asn Gly Val Asn
 180 185 190

Gln Ala Ser Lys Glu Ala Asn Gln Leu Leu Asn Gly Asn His Gln Ser
 195 200 205

Gly Ser Ser Ser His Gln Gly Gly Ala Thr Thr Thr Pro Leu Ala Ser
 210 215 220

Gly Ala Ser Val Asn Thr Pro Phe Ile Asn Leu Pro Ala Leu Trp Arg
 225 230 235 240

Ser Val Ala Asn Ile Met Pro Xaa
 245

<210> 267

<211> 178

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (155)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (178)

<223> Xaa equals stop translation

<400> 267

Met Leu Phe Leu Phe Leu Tyr Cys Leu Leu Val Val Leu Pro Phe Lys
 1 5 10 15

Leu Thr Pro Lys His Ser Ala Glu Val Leu Leu Ser Ile His Lys Ser
 20 25 30

Lys Lys Tyr Leu Cys Lys Val Lys Ala Ala Cys Lys Ile Gln Ala Trp
 35 40 45

Tyr Arg Cys Trp Arg Ala His Lys Glu Tyr Leu Ala Ile Leu Lys Ala
 50 55 60

Val Lys Ile Ile Gln Gly Cys Phe Tyr Thr Lys Leu Glu Arg Thr Arg
 65 70 75 80

Phe Leu Asn Val Arg Ala Ser Ala Ile Ile Ile Gln Arg Lys Trp Arg
 85 90 95

Ala Ile Leu Pro Ala Lys Ile Ala His Glu His Phe Leu Met Ile Lys
 100 105 110

Arg His Arg Ala Ala Cys Leu Ile Gln Ala His Tyr Arg Gly Tyr Lys
 115 120 125

Gly Arg Gln Val Phe Leu Arg Gln Lys Ser Ala Ala Leu Ile Ile Gln
 130 135 140

Lys Tyr Ile Arg Ala Arg Glu Ala Gly Lys Xaa Glu Arg Ile Lys Tyr
 145 150 155 160

Ile Glu Phe Lys Asn Leu Gln Leu Ser Tyr Lys His Trp Cys Val Val
 165 170 175

Gly Xaa

<210> 268

<211> 79

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (79)

<223> Xaa equals stop translation

<400> 268

Met Arg Pro Leu Leu Gly Leu Leu Leu Val Phe Ala Gly Cys Thr Phe
 1 5 10 15

Ala Leu Tyr Leu Leu Ser Thr Arg Leu Pro Arg Gly Arg Arg Leu Gly
 20 25 30

Ser Thr Glu Glu Ala Gly Gly Arg Ser Leu Trp Phe Pro Ser Asp Leu
 35 40 45

Ala Glu Leu Arg Glu Leu Ser Glu Val Leu Arg Glu Tyr Arg Lys Glu
 50 55 60

His Gln Ala Tyr Val Phe Leu Leu Phe Cys Gly Ala Tyr Leu Xaa
 65 70 75

<210> 269

<211> 81

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (81)

<223> Xaa equals stop translation

<400> 269

Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys
 1 5 10 15

Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
 20 25 30

Phe Gln Asp Thr Lys Val Tyr Cys Thr Arg Glu Ser Asn Pro His Cys

35

40

45

Gly Ser Asp Gly Gln Thr Tyr Gly Asn Lys Cys Ala Phe Cys Lys Ala
 50 55 60

Ile Val Lys Ser Gly Gly Lys Ile Ser Leu Lys His Pro Gly Lys Cys
 65 70 75 80

Xaa

<210> 270

<211> 69

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (69)

<223> Xaa equals stop translation

<400> 270

Met Asp Ala Ala Met Pro Val Cys Pro Cys Leu Ile Cys Val Cys Phe
 1 5 10 15

Val Leu Arg Leu Gln Ser Gly Val Ala Gly Thr Glu Thr Glu Arg Pro
 20 25 30

Pro His Gly Ala Ala Ser Leu His Gln Asp Arg Gly Ala Thr Leu Arg
 35 40 45

Leu Cys Phe Phe Pro Ser Gly Val Gly Phe Leu Leu Phe Leu Ser Ile
 50 55 60

Leu Pro Trp Ser Xaa
 65

<210> 271

<211> 131

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (131)

<223> Xaa equals stop translation

<400> 271

Met Asn Phe Arg Gln Arg Met Gly Trp Ile Gly Val Gly Leu Tyr Leu
 1 5 10 15

Leu Ala Ser Ala Ala Ala Phe Tyr Tyr Val Phe Glu Ile Ser Glu Thr
 20 25 30

Tyr Asn Arg Leu Ala Leu Glu His Ile Gln Gln His Pro Glu Glu Pro
 35 40 45

Leu Glu Gly Thr Thr Trp Thr His Ser Leu Lys Ala Gln Leu Leu Ser
50 55 60

Leu Pro Phe Trp Val Trp Thr Val Ile Phe Leu Val Pro Tyr Leu Gln
55 70 75 80

Met Phe Leu Phe Leu Tyr Ser Cys Thr Arg Ala Asp Pro Lys Thr Val
85 90 95

Gly Tyr Cys Ile Ile Pro Ile Cys Leu Ala Val Ile Cys Asn Arg His
100 105 110

Gln Ala Phe Val Lys Ala Ser Asn Gln Ile Ser Arg Leu Gln Leu Ile
115 120 125

Asp Thr Xaa
130

<210> 272

<211> 85

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (65)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (85)

<223> Xaa equals stop translation

<400> 272

Met Trp Val Phe Phe Leu Pro Phe Phe Ser Ile Leu Phe Lys Ile Cys
1 5 10 15

Trp Cys Ile Ser Leu Ser Gln Thr Lys Glu Lys Gln Ser Ser Asn Leu
20 25 30

Met Phe Tyr Phe Phe Cys Ile Cys Thr Tyr Glu Arg Arg Arg Lys Lys
35 40 45

Glu Met Arg Arg Gly Glu Lys Lys Arg Ser Phe Cys Leu Ile Gly Leu
50 55 60

Xaa Gln His Met Ile Ala Val Gln Ala Trp Phe His Glu Gln His Gln
65 70 75 80

Ile Gln Ile Ser Xaa
85

<210> 273

<211> 79

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (61)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (79)

<223> Xaa equals stop translation

<400> 273

Met Gln Trp Pro Phe Leu Cys Val Leu Pro Leu Leu Pro Gln Val Trp
1 5 10 15

Arg Ala Gly Ser Leu Leu Arg Ala Leu Glu Leu Tyr Ser Val Leu Leu
20 25 30

Ser His Phe Leu Trp Glu Met Trp Thr Met Ser Leu Lys Glu Pro Glu
35 40 45

Leu Leu Leu Ser Thr Lys Ser Leu Thr Val Trp Arg Xaa Arg Glu Pro
50 55 60

Leu Ser Glu Ile Gly Gly Cys Arg Leu Asn Asn Glu Gly Thr Xaa
65 70 75

<210> 274

<211> 54

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (54)

<223> Xaa equals stop translation

<400> 274

Met Phe Cys Phe Asn Trp Leu Leu Cys Phe Leu Phe Pro Arg Phe Pro
1 5 10 15

Ile Leu Val Cys Arg Lys His Gln Phe Cys Val Tyr Leu Leu Leu Val
20 25 30

Leu Lys Leu Arg Thr Leu Tyr Ala Glu Leu Ile Asp Leu His Leu Cys
35 40 45

Ala Ser Ile Leu Gly Xaa
50

<210> 275

<211> 155

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (150)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (155)

<223> Xaa equals stop translation

<400> 275

Met	Ala	Arg	His	Gly	Leu	Pro	Leu	Leu	Pro	Leu	Leu	Ser	Leu	Leu	Val
1				5					10					15	

Gly	Ala	Trp	Leu	Lys	Leu	Gly	Asn	Gly	Gln	Ala	Thr	Ser	Met	Val	Gln
			20					25					30		

Leu	Gln	Gly	Gly	Arg	Phe	Leu	Met	Gly	Thr	Asn	Ser	Pro	Asp	Ser	Arg
		35					40						45		

Asp	Gly	Glu	Gly	Pro	Val	Arg	Glu	Ala	Thr	Val	Lys	Pro	Phe	Ala	Ile
	50					55						60			

Asp	Ile	Phe	Pro	Val	Thr	Asn	Lys	Asp	Phe	Arg	Asp	Phe	Val	Arg	Glu
	65				70					75					80

Lys	Lys	Tyr	Arg	Thr	Glu	Ala	Glu	Met	Phe	Gly	Trp	Ser	Phe	Val	Phe
				85					90					95	

Glu	Asp	Phe	Val	Ser	Asp	Glu	Leu	Arg	Asn	Lys	Ala	Thr	Gln	Pro	Met
			100					105					110		

Lys	Ser	Val	Leu	Trp	Trp	Leu	Pro	Val	Glu	Lys	Ala	Phe	Trp	Arg	Gln
		115				120							125		

Pro	Ala	Gly	Pro	Gly	Ser	Gly	Ile	Arg	Glu	Arg	Leu	Glu	His	Pro	Val
	130					135					140				

Leu	His	Val	Ser	Trp	Xaa	Asp	Ala	Arg	Ala	Xaa
145					150					155

<210> 276

<211> 129

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (68)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (98)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (103)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (104)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (112)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (114)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (129)
<223> Xaa equals stop translation

<400> 276
Met Ala Tyr Arg His Phe Trp Met Leu Val Leu Phe Val Ile Phe Asn
1 5 10 15
Ser Leu Gln Gly Leu Tyr Val Phe Met Val Tyr Phe Ile Leu His Asn
20 25 30
Gln Met Cys Cys Pro Met Lys Ala Ser Tyr Thr Val Glu Met Asn Gly
35 40 45
His Pro Gly Pro Ser Thr Ala Phe Phe Thr Pro Gly Ser Gly Met Pro
50 55 60
Pro Ala Gly Xaa Glu Ile Ser Lys Ser Thr Gln Asn Leu Asn Arg Trp
65 70 75 80
Tyr Gly Gly Arg Cys His Leu Thr Gly Arg Glu His Pro Ser Lys Gln
85 90 95
Gly Xaa Gln Gly Gln Pro Xaa Xaa Lys Ala Lys Ser Thr Lys Trp Xaa
100 105 110
His Xaa Pro Val Leu Trp Arg Ile Trp Pro Gly Xaa Thr Asp Ser Arg
115 120 125
Xaa

<210> 277
 <211> 84
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (84)
 <223> Xaa equals stop translation

<400> 277
 Met Ala Ser Pro Gly Trp His Leu Ser Cys Arg Pro Thr Gly Leu Val
 1 5 10 15
 Ser Ile Phe Leu Leu Cys Ala Pro Ala Tyr Leu His Ser Phe Val Met
 20 25 30
 Thr Ser Ile Thr Leu Ile Ser Thr Lys Ile Cys Ser Pro Thr Lys Leu
 35 40 45
 Arg His Arg Thr His Phe Leu Tyr Gly Ser Ile Met Glu Leu Tyr Pro
 50 55 60
 Thr Leu Thr Phe Pro Met Thr Thr Asp Val Glu Asn Leu Asn Leu Asp
 65 70 75 80
 Ser Ser Arg Xaa

<210> 278
 <211> 86
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (86)
 <223> Xaa equals stop translation

<400> 278
 Met Gly Cys Arg Gly Asn Lys Leu Phe Val Leu Ser Tyr Cys Thr Cys
 1 5 10 15
 Leu Thr Trp Leu Leu Gly Thr Lys Ser Gln Lys Asn Pro Phe Gln Val
 20 25 30
 Cys Met Ser Gly Gly Trp Ala Val Ser Arg Leu Glu Thr Gly Phe Gln
 35 40 45
 Ala Leu His Asp Gly Arg Ala Ser Ser Pro Leu Ser Ala Ala Cys Val
 50 55 60
 Leu Asp Arg Thr Val Ala Arg Arg Trp Lys Pro Pro Ser Val Pro Leu
 65 70 75 80
 Ala His His Thr Lys Xaa
 85

<210> 279
<211> 96
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (96)
<223> Xaa equals stop translation

<400> 279
Met Pro Trp Leu Thr Ile Leu Arg Phe Leu Gln Ala Ser Gly His Val
1 5 10 15
Arg Ala Gln Asp Leu Ala Leu Leu Gly Asp Thr Ser Val Cys Ile Arg
20 25 30
Cys Gly Cys Gly Gly Cys Ser Leu Ser Ile Ala Asn Tyr Glu Trp Val
35 40 45
Pro Leu Arg Arg Lys Asp Cys Lys Arg Tyr Glu Thr Ser Glu Lys Thr
50 55 60
Ser Cys Leu Leu Leu Pro Ser Ala Cys Ser Arg Gln Asn Ala Val Gly
65 70 75 80
Phe Ser Arg Leu Pro Val Pro Lys Leu Ser Cys Leu Leu His Gly Xaa
85 90 95

<210> 280
<211> 98
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (70)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (98)
<223> Xaa equals stop translation

<400> 280
Met Ile Leu Leu Phe Leu Leu Ser Leu Ser Leu Ser Leu Ser Leu
1 5 10 15
Ser Leu Ser Phe Ser Pro Leu Asn Cys Leu Phe Ser Phe Trp Gly Ser
20 25 30
Pro Pro Thr Arg Cys Ser Trp Cys Arg Leu Gly Ser Gln Gly Glu Ala

35

40

45

Trp Trp Pro Gly Leu Gly Arg Gly Thr Leu Ser Leu Ala Lys Ala Glu
 50 55 60

Ser Glu Ile Val Val Xaa Leu Cys Lys Ser Tyr Phe Gln Tyr Phe Leu
 65 70 75 80

Ala Ala Ser Glu Val Ser Leu Thr Pro Cys Arg Ala Leu Leu Leu Leu
 85 90 95

Ser Xaa

<210> 281

<211> 55

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (55)

<223> Xaa equals stop translation

<400> 281

Met Ser Val Trp Pro Arg Ser Thr Leu Leu Phe Cys Leu Leu Ser Leu
 1 5 10 15

Ser Thr Gly Leu Phe Leu Asp Lys Leu Gly Ile Ile Ile Pro Ile Leu
 20 25 30

Leu Cys Gly Trp Lys Leu Asn Val Ile Met Met Cys Val Arg Cys Leu
 35 40 45

His Ser Ala Trp Arg Tyr Xaa
 50 55

<210> 282

<211> 72

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (72)

<223> Xaa equals stop translation

<400> 282

Met Arg Ile His Phe Lys Ile Leu Val Leu Val Ile Tyr Phe Ile Leu
 1 5 10 15

Leu Gly Ser Phe Ser Asp Arg Cys Ser Leu Leu Asp Cys Lys Ser Arg
 20 25 30

Ile Gln Arg Ile Phe Ile Cys Asn Ile Leu Asn Leu Ser Leu Val Ser
 35 40 45

Cys His Leu Cys Arg Tyr Ser Phe Asp Cys Leu Thr Arg Gly Lys Cys
50 55 60

Phe Pro Leu Ser Phe Pro Ala Xaa
65 70

<210> 283
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 283
Met Tyr Ala Ala Ala Leu Ser Thr Ala Pro Ser Leu Phe Phe Leu His
1 5 10 15

Leu Cys Leu Leu Lys Thr Leu Ile Leu Phe Ser Leu Ser Ser Ile Pro
20 25 30

Leu Pro Pro Leu Leu Tyr Ser Tyr Asp Leu His Xaa
35 40

<210> 284
<211> 56
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (56)
<223> Xaa equals stop translation

<400> 284
Met Leu Pro Ser Asn Trp Ser Gly Thr Trp Ala Leu Ile Gln Leu Ser
1 5 10 15

Ile Pro Phe Thr Leu Ala Phe His Gln Pro Asn Lys Asn Gln Leu Thr
20 25 30

Gln Lys Lys Arg Lys Ala Pro Gln Gly Ser Phe Asp Pro Asp Ile Tyr
35 40 45

Ile Asp Ala Ile Gly Val Pro Xaa
50 55

<210> 285
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 285

Met Ser Thr Leu Arg Arg Met Ala Leu Leu Tyr Ile Glu Thr Pro Leu
1 5 10 15

Leu Arg Ala Leu Met Val Gln Gly Pro Arg Leu Val Ser Val Arg Ala
20 25 30

Ala Met His Gly Lys Cys Gly Gly Arg Ala Leu Trp Ala Leu Trp Gln
35 40 45

Xaa

<210> 286
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 286

Met Val Cys Val Arg Cys Val Trp Tyr Val Trp His Val Phe Gly Val
1 5 10 15

Tyr Gly Asn Ile Leu Trp Ile Arg Thr Cys Gly Leu Phe Lys Asp Leu
20 25 30

Ser Phe Cys Ala Leu Lys Ser Glu Met Xaa
35 40

<210> 287
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 287

Met Arg His Val Ala Ile Val Thr Met Ile Val Val Leu Ser Pro Pro
1 5 10 15

Val Leu Ala Ser Ser Leu Lys Pro Pro Leu Phe Ile Asp Thr Tyr Phe
20 25 30

Met Phe Gly Lys Arg Cys Ser Arg Trp Asp Thr Pro Ala Cys Ser Lys

35

40

45

Xaa

<210> 288

<211> 110

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (110)

<223> Xaa equals stop translation

<400> 288

Met Trp Ala Glu Leu Lys Leu Leu Ser Trp Gly Arg Ala Ala Ile Ala
1 5 10 15

Val Trp Val Cys Leu Arg Arg Val Val Arg Gly Gly His Ser Pro Pro
20 25 30

Ala Gly Gln Gly Gly Gln Gly Val Lys Val Gln Trp Glu Gly Val Gln
35 40 45

Gly Ser Gly Ser Gly Gln Pro Glu Asp Met Arg Trp Glu Lys Leu His
50 55 60

Val Arg Ile Leu Met Gln Gly Met His Gly Ala Pro Gln Asp Asp Ile
65 70 75 80

Arg Ser Val His Gly Ser Thr Ala Phe Pro Asp Cys Leu His Leu Pro
85 90 95

Cys Arg Pro Thr Cys Pro Gly Val Ser Phe Gly Ser Gly Xaa
100 105 110

<210> 289

<211> 64

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (64)

<223> Xaa equals stop translation

<400> 289

Met Leu Leu Val Ser Cys Phe Met Ser Ile Tyr Phe Leu Ser Pro Leu
1 5 10 15

Leu Leu Pro Leu His Gly Ser Pro His Pro His Ser Tyr Leu Cys Phe
20 25 30

Ala Val Cys Arg Thr Ser Trp Ser Leu Ser Glu Lys Thr Cys Asn Phe
35 40 45

Pro Asn Glu Met Leu Gln Leu Pro Ile Phe Leu Lys Ser Ile Tyr Xaa
 50 55 60

<210> 290
 <211> 42
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (42)
 <223> Xaa equals stop translation

<400> 290
 Met Gly Leu Leu Leu Leu Leu Leu Leu Gly Cys Trp Thr His Ile Phe
 1 5 10 15

Phe Thr Asn Gly Met Ile Tyr Trp Tyr Leu Glu Gly His Pro Ile Leu
 20 25 30

Asn Glu Ile Leu Phe Ile Leu His Phe Xaa
 35 40

<210> 291
 <211> 43
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (43)
 <223> Xaa equals stop translation

<400> 291
 Met Ile Asn Cys Val Cys Val His Ala Cys Val Arg Ala Cys Gly Leu
 1 5 10 15

Leu His Ser Leu Val Leu Leu Leu Ser Leu Ser Leu Ser Ser Ala Leu
 20 25 30

Phe Ile Pro Trp Asp Thr Glu Ile Phe Lys Xaa
 35 40

<210> 292
 <211> 45
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (45)

<223> Xaa equals stop translation

<400> 292

Met Leu Phe Phe Cys Leu Leu Met Lys Met Leu Gly Pro Ser Arg Leu
1 5 10 15

Pro Phe Leu Ala Leu Thr Leu Cys Arg Phe Ile Leu Tyr Phe Gln Phe
20 25 30

Cys Tyr Leu Ile Ser Asp Ser Ser Pro Asp His Ser Xaa
35 40 45

<210> 293

<211> 57

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (57)

<223> Xaa equals stop translation

<400> 293

Met Cys Phe Thr Gln Phe Ser Arg Ile Phe Phe Leu Thr Ser Ser Leu
1 5 10 15

Thr Leu Ala Ala Cys Ala Asn His Ile Leu Ala Ala Tyr Ser Ser Ser
20 25 30

Leu Ala Asp Arg Cys Val Gly Glu Lys Ser Leu Ile Val Ile Val Pro
35 40 45

Glu Arg Ser Phe Gln Thr His Phe Xaa
50 55

<210> 294

<211> 75

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (75)

<223> Xaa equals stop translation

<400> 294

Met Met Tyr Val Gln Ser Ala Ile Met Ser Leu Gln His Leu Leu Val
1 5 10 15

Leu His Arg Val Ile Ile Ile Ser Met His Phe Ala Phe Gly Asn Gly
20 25 30

Cys Thr Phe Lys Ile Leu Val Gln Cys Ala Ile Arg Lys Tyr Thr Ser
35 40 45

Lys Met Ile Ser Arg Ile Ile Gln Met Tyr Leu Thr Thr Met Asp Leu

50

55

60

Phe His Pro Met Lys Leu Gln Arg Lys Leu Xaa
 55 70 75

<210> 295
 <211> 51
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (51)
 <223> Xaa equals stop translation

<400> 295
 Met Ile Ile Pro Lys Phe Tyr Leu Phe Lys Leu Leu Leu Leu Gln
 1 5 10 15

Lys Ile Thr His Phe Ile Cys Gly Lys Thr Leu Asn Asn Leu Asn Phe
 20 25 30

Arg Cys Glu Ser Tyr Phe Leu Phe Leu Tyr Leu Tyr Cys Ala Tyr Ile
 35 40 45

Leu Tyr Xaa
 50

<210> 296
 <211> 45
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (45)
 <223> Xaa equals stop translation

<400> 296
 Met Thr Gln Glu Ile Leu Val Val Phe Ser Ile Gln Val Leu Ser Ser
 1 5 10 15

Leu Arg Leu Leu Gly Leu Trp Phe Phe Met Glu Asn Arg Leu Cys Ser
 20 25 30

Gly Ile Val Glu Gln Arg Arg Leu Leu His Leu Asn Xaa
 35 40 45

<210> 297
 <211> 48
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE

<222> (48)

<223> Xaa equals stop translation

<400> 297

Met Pro Thr Leu Gly Asp Ala Leu Ile Leu Tyr Leu His Leu Val Leu
1 5 10 15

Gly Val Ala Gly Val Leu Gln Pro Pro Gly Pro Arg Pro Ser Gln Ala
20 25 30

Leu Gly Pro Thr Gly Asp Arg Ala Pro Gly Lys Trp Asn Arg Ser Xaa
35 40 45

<210> 298

<211> 55

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (55)

<223> Xaa equals stop translation

<400> 298

Met Ala Trp Cys Leu Leu Ser Val Phe Phe Leu Arg Ala Leu Cys Ala
1 5 10 15

His Ser Ser Thr Ala Tyr Lys Cys Val Leu Cys Ser Pro Arg Ser Pro
20 25 30

Trp Leu Val Glu Ala Asn Phe Trp Leu Asp Phe Tyr Gly Lys Ser Tyr
35 40 45

Phe Met Ser Pro Lys His Xaa
50 55

<210> 299

<211> 30

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (30)

<223> Xaa equals stop translation

<400> 299

Met Gln Met Thr Val Val Trp Tyr Val Ile Thr Ala Ile Ile Trp Trp
1 5 10 15

Arg Met Ser Met Cys Glu Ala Leu Ser Gln Asn Cys Phe Xaa
20 25 30

<210> 300
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (73)
<223> Xaa equals stop translation

<400> 300
Met Pro Leu Gly Val Val Pro Arg Ala Val Trp Ser Thr Leu Ala Trp
1 5 10 15
Val Cys Ile Ile Leu Gln Thr Leu Lys Thr Ser Leu Phe Cys Gln Thr
20 25 30
Thr Phe Cys Gly Glu Pro Glu Asp Ser Gly Phe Phe Glu Gly Ile Leu
35 40 45
Asp Val Cys Val Leu Val Lys Glu Ala Val Ile Arg Leu Asn His Asn
50 55 60
Pro Gln Asp Leu Leu Asp Ser Asp Xaa
65 70

<210> 301
<211> 37
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (37)
<223> Xaa equals stop translation

<400> 301
Met Leu Arg Leu Glu Val Leu Leu Leu Phe Phe Ser Lys Val Thr Asp
1 5 10 15
Gln Ile Ile Thr Gln Ile Ile Gln Glu Asn Arg Ser Glu Ile Lys Asn
20 25 30
Asn Ile Ile Phe Xaa
35

<210> 302
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 302

Met Arg Pro Val Leu Arg Arg Thr Phe Leu Leu Thr Leu Phe Ser Val
1 5 10 15

Ile Ala Leu Thr Lys Ile Lys His Asp Phe Phe Ile Met Cys Ser His
20 25 30

Met Gln Cys Ile Pro Arg Val Phe Leu Lys His Glu Phe Asn Asn Ile
35 40 45

Xaa

<210> 303

<211> 42

<212> PRT

<213> Homo sapiens

<400> 303

Met Phe Tyr Thr Thr Leu Cys Lys Met Phe Gln Tyr Leu His Ile Leu
1 5 10 15

Ser Leu Ser Phe Cys Phe Ala Leu Ile Trp Trp Ser Glu Ser Phe Leu
20 25 30

Trp Leu Ser Asn Leu Val Arg Leu Arg His
35 40

<210> 304

<211> 54

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (54)

<223> Xaa equals stop translation

<400> 304

Met Ile Leu Leu Ile Ser Gln Cys Pro Leu Ser Ile Phe Ala Ala Pro
1 5 10 15

Phe Ala Leu Pro Pro Lys Gly His Cys Gly Ser Phe Ser Asp Phe His
20 25 30

Ser Gln Val Thr Leu His Lys Asn Ser Lys Leu Ile Phe Arg Ser His
35 40 45

Lys Ser Ile Leu Leu Xaa
50

<210> 305

<211> 76

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (76)

<223> Xaa equals stop translation

<400> 305

Met Leu Ala Ala Glu Leu Ile Cys Cys Pro Ser Leu His Ile Phe Phe
1 5 10 15

Phe Ala Ala Phe Ser Leu Trp Gln Cys Thr Val Leu Thr Met Pro Phe
20 25 30

Lys Asn Val Pro Tyr Cys Ile Ser Ile Leu Arg Arg Asp Arg Thr Lys
35 40 45

Lys Tyr Ile Ala Gln Ile Ile Phe Tyr Phe Ile Asp Asn Asp Lys Glu
50 55 60

Tyr Phe Leu Asn Pro Ile Lys Ile Asp Phe Asn Xaa
65 70 75

<210> 306

<211> 63

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (63)

<223> Xaa equals stop translation

<400> 306

Met Phe Phe Arg Met Gln Val Cys Glu His His Gly Phe Trp Val Ile
1 5 10 15

Leu Leu Leu Leu Ser Leu Lys Met Glu Ile Pro Leu Ala Ala Tyr Pro
20 25 30

Thr Ala Glu Tyr Ser Ser Ile Gly Ser Gly Phe Thr Pro Leu His Pro
35 40 45

Ser Arg Thr Phe Thr Gln Ala Ser Pro Leu Pro Ser Ile Phe Xaa
50 55 60

<210> 307

<211> 50

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (50)

<223> Xaa equals stop translation

<400> 307

Met Asn Val Phe Val Gly Pro Leu Ser Val Ala Ile Val Ile Phe Cys
1 5 10 15

Trp Ile Thr Met Tyr Trp Val Ser Ile Val Met Gly Gln Gly Arg Gly
20 25 30

Gln Tyr Thr Trp Arg Thr Ile Leu Ser Thr Ser Thr Pro Ser Val Cys
35 40 45

Ser Xaa
50

<210> 308

<211> 103

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (103)

<223> Xaa equals stop translation

<400> 308

Met Glu His Trp Ile Pro Pro Glu Val Pro Leu Ala Gly Leu Arg Arg
1 5 10 15

Leu Leu Leu Asp Arg Leu Val Phe Ala Pro Ala Phe Leu Met Leu Phe
20 25 30

Phe Leu Ile Met Asn Phe Leu Glu Gly Lys Asp Ala Ser Ala Phe Ala
35 40 45

Ala Lys Met Arg Gly Gly Phe Trp Pro Ala Leu Arg Met Asn Trp Arg
50 55 60

Val Trp Thr Pro Leu Gln Phe Ile Asn Ile Asn Tyr Val Pro Leu Lys
65 70 75 80

Phe Arg Val Leu Phe Ala Asn Leu Ala Ala Leu Phe Trp Tyr Ala Tyr
85 90 95

Leu Ala Ser Leu Gly Lys Xaa
100

<210> 309

<211> 45

<212> PRT

<213> Homo sapiens

<400> 309

Met Arg Phe Ile Ser Gln Gln Ser Cys Glu Cys Val Arg Pro Cys Met
1 5 10 15

Asp Val Tyr Val Cys Val Tyr Ile Ser Ile His Val Tyr Met Asp Ala
20 25 30

His Val Tyr Leu Cys Arg Ile Cys Lys Thr Asn Met Arg
 35 40 45

<210> 310

<211> 53

<212> PRT

<213> Homo sapiens

<400> 310

Arg Ile Leu Arg Trp Val Asn Cys Met Ala Cys Asp Leu Tyr Leu Asn
 1 5 10 15

Lys Ala Val Ser Val Cys Ala His Val Trp Met Cys Met Cys Val Tyr
 20 25 30

Ile Ser Leu Tyr Met Tyr Thr Trp Met Pro Met Cys Ile Tyr Val Glu
 35 40 45

Tyr Val Lys Gln Thr
 50

<210> 311

<211> 59

<212> PRT

<213> Homo sapiens

<400> 311

Asn Pro Glu Asn Gln Leu Glu Ile Ser Phe Pro Pro Arg Arg Gln Lys
 1 5 10 15

Met Lys Leu Thr Leu Asp Leu Gln Val Ser Gln Ser Ser Leu Val His
 20 25 30

Ser Leu Leu Ser Ser Asp Phe Phe Ser Val Ser Lys Glu Gly Cys Leu
 35 40 45

Trp Lys Pro Ile Leu Leu Pro Ser His Phe Leu
 50 55

<210> 312

<211> 47

<212> PRT

<213> Homo sapiens

<400> 312

Leu Gln Thr Gln Ile Ser Asn Tyr Leu Met Phe Val Leu His Ile Leu
 1 5 10 15

His Arg Tyr Thr Trp Ala Ser Met Tyr Thr Cys Ile Glu Ile Tyr Thr
 20 25 30

His Thr Tyr Thr Ser Ile His Gly Arg Thr His Ser Gln Leu Cys
 35 40 45

<210> 313
<211> 45
<212> PRT
<213> Homo sapiens

<400> 313
Ile His Met Gly Ile His Val Tyr Met Tyr Arg Asp Ile Tyr Thr His
1 5 10 15
Ile His Ile His Thr Trp Ala His Thr Leu Thr Ala Leu Leu Arg Tyr
20 25 30
Lys Ser His Ala Ile Gln Leu Thr His Leu Asn Ile Arg
35 40 45

<210> 314
<211> 41
<212> PRT
<213> Homo sapiens

<400> 314
Met Lys Trp Ile Phe Thr Val Leu Ile Leu Thr Ser Cys Phe Phe Thr
1 5 10 15
Ala Gly Ile Cys Glu Asp Gly Ile Cys Ser Arg Ile Gln Leu Arg Asp
20 25 30
Lys Ile Val Gln Ser Ala Phe Arg Gln
35 40

<210> 315
<211> 81
<212> PRT
<213> Homo sapiens

<400> 315
Lys Pro Cys Cys Pro Ser Val Ser Asn Arg Ser Ser Val Gln Met His
1 5 10 15
Gln Leu Pro Ile Gln Phe Leu Gly Gln Phe Glu Ala His Cys Ile Gly
20 25 30
Phe Cys Arg Ser Phe Leu Glu Thr Phe Tyr Thr His Asp Pro Arg Ala
35 40 45
Met His Ser Phe Leu Ser Ser Ile Ser Ser Pro Ser Leu Pro Phe Gly
50 55 60
Phe Ser Arg Met Thr Ser Gln Ile Asn His Leu His Pro Ser Pro Leu
65 70 75 80
Cys

<210> 316
 <211> 21
 <212> PRT
 <213> Homo sapiens

<400> 316
 Ser Val Phe Lys Ile Asn Leu Lys Ser Phe Lys Gln His Glu Pro Trp
 1 5 10 15
 Trp Pro Asn Arg Ser
 20

<210> 317
 <211> 135
 <212> PRT
 <213> Homo sapiens

<400> 317
 Gly Thr Arg Ser Phe Ser Val Pro Ser Tyr Leu Arg Leu Thr Gly Ser
 1 5 10 15
 Leu Met Cys Tyr Leu Leu Leu Leu Leu Ile Gln Thr Ala Glu Leu Leu
 20 25 30
 Ile His Pro Gln Gly Leu Gln Ala Val Ser Asn Gly Glu Ser Ala Leu
 35 40 45
 Lys Gly Thr Arg Pro Thr Phe Ser Ser Pro Phe Ile Leu Val Thr Glu
 50 55 60
 Gly Arg Lys Glu Trp Glu Gly Val Phe Leu Ser Ser Gly Trp Lys Gly
 65 70 75 80
 Asn Thr Leu Ser Asn Tyr Tyr Ile Ser Leu Val Phe Tyr Tyr Ser Arg
 85 90 95
 Ile Leu Gln Pro Tyr Phe Tyr Cys Leu Trp Gly Lys Leu Glu Met Val
 100 105 110
 Thr Leu Ile Arg Ser Val Trp Arg Gly Ile Asn Gly Gly Asp Lys Ile
 115 120 125
 Ser Val Gly Phe Gly Lys Cys
 130 135

<210> 318
 <211> 38
 <212> PRT
 <213> Homo sapiens

<400> 318
 Trp Met Glu Arg Lys His Thr Val Lys Leu Leu Tyr Leu Leu Gly Phe
 1 5 10 15
 Leu Leu Gln Asn Ser Pro Ala Ile Phe Leu Leu Ser Met Gly Glu Val
 20 25 30

Gly Asp Gly Asp Leu Asp
35

<210> 319
<211> 23
<212> PRT
<213> Homo sapiens

<400> 319
Ser Asn Gly Glu Ser Ala Leu Lys Gly Thr Arg Pro Thr Phe Ser Ser
1 5 10 15

Pro Phe Ile Leu Val Thr Glu
20

<210> 320
<211> 24
<212> PRT
<213> Homo sapiens

<400> 320
Leu Ser Asn Tyr Tyr Ile Ser Leu Val Phe Tyr Tyr Ser Arg Ile Leu
1 5 10 15

Gln Pro Tyr Phe Tyr Cys Leu Trp
20

<210> 321
<211> 131
<212> PRT
<213> Homo sapiens

<400> 321
Glu Lys Asp Phe Met Gln Gly Ser Asp Ala Gly His Gly Gly Thr His
1 5 10 15

Ile Tyr Arg Ala Leu Val Gln Trp Pro Leu Ala Trp Val Phe Tyr Leu
20 25 30

Ser His Ala Lys Thr His Trp Gly Glu Glu Leu Arg Phe Ser Phe Arg
35 40 45

Arg Lys Asn Leu Arg Leu Arg Glu Ala Met Arg His Glu Thr Cys Gln
50 55 60

Val Thr Gln Leu Val Ala Gly Lys Ala Asp Ser Asn Leu Cys Leu Arg
65 70 75 80

Asp Ser Glu Thr Trp Phe Trp Pro Pro Leu Trp Ala Ala Cys Ser Ser
85 90 95

Leu Gln Ala Thr Ala Cys Arg Leu Ser Ser Pro Ser Lys Gly Leu Gly
100 105 110

Ala Ser Arg Glu Cys Pro Trp Leu Ala Ser Gly Arg Ala Ala Leu Val
115 120 125

Ser Phe Leu
130

<210> 322
<211> 69
<212> PRT
<213> Homo sapiens

<400> 322
Ser Leu Arg Val Lys Gly Arg Lys Pro Arg Leu Leu Tyr His Ser Pro
1 5 10 15

Ala Arg Gly Thr Leu Trp Met Leu Pro Gly Leu Cys Asp Cys Leu Ile
20 25 30

Cys Arg Gln Trp Leu Val Glu Arg Ser Arg Leu Pro Arg Val Gly Ala
35 40 45

Arg Thr Arg Phe Gln Ser Pro Ser Asp Thr Gly Trp Ser Gln Leu Cys
50 55 60

Gln Leu Pro Ala Val
65

<210> 323
<211> 26
<212> PRT
<213> Homo sapiens

<400> 323
Glu Arg Ser Arg Leu Pro Arg Val Gly Ala Arg Thr Arg Phe Gln Ser
1 5 10 15

Pro Ser Asp Thr Gly Trp Ser Gln Leu Cys
20 25

<210> 324
<211> 33
<212> PRT
<213> Homo sapiens

<400> 324
Lys His Ala Phe Leu Met Ala His Gln Phe Cys Val Leu Ser Leu Ala
1 5 10 15

Met Gln Trp Ser Ser Cys Phe Gln Leu Val Ala Leu Pro Tyr Leu Ser
20 25 30

Leu

<210> 325
<211> 51
<212> PRT
<213> Homo sapiens

<400> 325
Met Arg Pro Leu Cys Val Leu Leu Pro Trp Pro Cys Trp Gln Trp Gly
1 5 10 15
Gly Leu Gly Ser Ala Ser Pro Ile Arg Pro Gln Ala Pro Pro Gly Gln
20 25 30
Ala Ala His Ala Val Pro Leu Pro Arg Ala Gln His Leu Ala Gln Arg
35 40 45
Ser Arg Gln
50

<210> 326
<211> 52
<212> PRT
<213> Homo sapiens

<400> 326
Ala Arg Gly Leu Arg Ser Pro His Gly Ala Ala Gly Val Val Arg Gly
1 5 10 15
Asp Gly Gly Gly Lys Lys Gly Glu Asp Pro Tyr Ser Pro Ile Leu Phe
20 25 30
Gln Ser Glu Arg Ile Pro Arg Leu Ile Tyr Leu Pro Val Ile Ser Ser
35 40 45
Glu Glu Asn Ser
50

<210> 327
<211> 57
<212> PRT
<213> Homo sapiens

<400> 327
Lys Ser Leu Ser Cys Ser Phe Leu Phe Leu Ala Phe Trp Leu Arg Arg
1 5 10 15
Met Gly Gln Thr Met Cys Val Cys Val Cys Val Cys Val Cys Val Cys
20 25 30
Val Arg Thr Trp Val Tyr Leu Tyr Glu Pro Val Lys Phe Arg Ser Pro
35 40 45
Leu Ile Tyr Val Asn Leu Pro Thr Ser
50 55

<210> 328

<211> 80
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (15)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 328

Lys Leu Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser Xaa Thr
 1 5 10 15

Ser Gly Asp Leu Pro Ser Ser Ala Ser Gln Asn Ala Gly Ile Lys Gly
 20 25 30

Met Ser Tyr Arg Ala Trp Pro Tyr Ser Tyr Phe Leu Ile Arg Lys Asn
 35 40 45

Lys Gln Thr Asn Lys Gln Thr Lys Thr Asn Pro Gln Leu Gly Glu Asn
 50 55 60

Lys His Cys Arg Asn Leu Lys Val Ser Trp Ser Lys Asn Tyr Phe Leu
 65 70 75 80

<210> 329
 <211> 27
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (25)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 329

Glu Arg Gly Gln Gly Gly Ser Ser Arg Asn Val Ala Gly Ser Asp Leu
 1 5 10 15

Val Phe Pro Ala Val Phe Val Ser Xaa Leu Cys
 20 25

<210> 330
 <211> 166
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (90)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
 <222> (92)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (96)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (113)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (126)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (141)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <220>
 <221> SITE
 <222> (150)
 <223> Xaa equals any of the naturally occurring L-amino acids

 <400> 330
 Gly Ser Pro Gln Gly Pro Ser Val Ala Leu Gly Ser Arg Gln Cys Trp
 1 5 10 15
 Ser Arg Pro Leu Arg Arg Gly Gly Arg Gly Ala Ala Val Glu Met Trp
 20 25 30
 Arg Gly Pro Thr Trp Cys Phe Arg Pro Ser Leu Cys Leu Cys Cys Val
 35 40 45
 Cys Gly Val Ser Phe Gly Leu Tyr Val Pro His Gly Phe Ser Leu Ser
 50 55 60
 Met Cys Val Ser Ala Pro Gly Ser Ala Trp Leu Ser Leu Val Tyr Ser
 65 70 75 80
 Ile Cys Leu Ala Arg Gly Ser Met Ser Xaa Arg Xaa Ser Ser Arg Xaa
 85 90 95
 Ser Leu Val Ala Ser Gly Ala Ser Val Leu Leu Val Cys Phe Trp Val
 100 105 110
 Xaa Ala Asp Pro Gly Val Gly Val Ser Val Pro Arg Ala Xaa Val Ser
 115 120 125
 Gly Leu Trp Trp Cys Val Ser Pro Ser Ala Cys Leu Xaa Leu Ala Pro
 130 135 140
 Thr Lys Pro Pro Pro Xaa Leu Ser Phe Ser Leu Ser Ile Phe Pro Phe

145

150

155

160

Ser Ser Asn Pro Ser Lys
165

<210> 331
<211> 118
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (39)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (55)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (67)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (89)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 331
Thr Ile Ala Ser Leu Gln Pro Thr Ala Leu Asn His Leu Ile Trp Arg
1 5 10 15

Gly Trp Lys Arg Lys Gly Arg Leu Arg Glu Arg Lys Arg Gly Xaa Gly
20 25 30

Gly Ala Trp Leu Gly Pro Xaa Arg Gly Arg Gln Met Asp Ser His Thr
35 40 45

Thr Arg Asp Gln Arg Gln Xaa Leu Gly Glu Gln Arg His Pro Leu Leu
50 55 60

Gly Leu Xaa Ala Pro Arg Ser Lys Pro Thr Lys Gln Met Pro Gln Met
65 70 75 80

Gln Pro Gly Xaa Pro Glu Lys Lys Xaa Xaa Leu Thr Trp Asn His Gly
85 90 95

Leu Asp Arg Trp Asn Thr Gln Gly Thr Ala Arg Gln Ser Leu Gly Gln
100 105 110

Lys His Thr Trp Arg Asp
115

<210> 332

<211> 21

<212> PRT

<213> Homo sapiens

<400> 332

Ala Arg Gly Pro Gly Thr Glu Gly Cys Glu Pro Trp Leu Gln Leu Gln
1 5 10 15

Asp Arg Arg Glu Arg
20

<210> 333

<211> 59

<212> PRT

<213> Homo sapiens

<400> 333

Met Ser Ser Gly Thr Asn Ser Phe Phe Thr Leu Met Ala Leu Asn Ser
1 5 10 15

Pro Thr Gly Asp Ser Gly Ser Arg Ile Thr Val Ser Pro Pro Arg Val
20 25 30

His Pro Val Lys Ser Gly Arg Gly Arg Ala Ser Asp Leu Leu Leu Thr
35 40 45

Arg Phe Leu Ala Pro Arg Ser Ala Leu Trp Ser
50 55

<210> 334

<211> 26

<212> PRT

<213> Homo sapiens

<400> 334

His Glu Tyr His Leu Leu Ser Ser Arg His Ile Leu Gly Ser Val Leu
1 5 10 15

Arg Leu Asp Val Cys Ser Ala Leu Trp Ser
20 25

<210> 335
 <211> 82
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (44)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (54)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (59)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (67)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 335
 Phe Ile Leu Phe Ile Leu Glu Tyr Asp Met Leu Trp Lys Ser Leu Tyr
 1 5 10 15
 Thr Asn Ser Ser Ala Tyr Gly Tyr Val Ile Ala Ser Tyr Phe Cys Leu
 20 25 30
 Leu Gly Ile Lys Leu Leu Val Lys Gln Lys Lys Xaa Lys Lys Lys Thr
 35 40 45
 Arg Gly Gly Ala Arg Xaa Pro Ile Arg Pro Xaa Val Glu Ser Tyr Tyr
 50 55 60
 Lys Ser Xaa Ala Val Val Leu Gln Arg Arg Gly Leu Gly Lys Asn Leu
 65 70 75 80
 Gly Gly

<210> 336
 <211> 102
 <212> PRT
 <213> Homo sapiens

<400> 336
 Arg Val Ser Ser His Leu Phe Arg Leu Phe Gly Gly Leu Ile Leu Asp
 1 5 10 15
 Ile Lys Arg Lys Ala Pro Phe Phe Leu Ser Asp Phe Lys Asp Ala Leu
 20 25 30

Ser Leu Gln Cys Leu Ala Ser Ile Leu Phe Leu Tyr Cys Ala Cys Met
35 40 45

Ser Pro Val Ile Thr Phe Gly Gly Leu Leu Gly Glu Ala Thr Glu Gly
50 55 60

Arg Ile Val Ser Thr Lys Ile Gly Ser Gly Gln Ala Phe Ser Ser Ser
65 70 75 80

Glu Ala Ser Val Cys Met His Leu Ser His Tyr Ser Tyr Phe Tyr Leu
85 90 95

Lys Ser Leu Pro Thr Ala
100

<210> 337

<211> 24

<212> PRT

<213> Homo sapiens

<400> 337

Phe Arg Leu Phe Gly Gly Leu Ile Leu Asp Ile Lys Arg Lys Ala Pro
1 5 10 15

Phe Phe Leu Ser Asp Phe Lys Asp
20

<210> 338

<211> 23

<212> PRT

<213> Homo sapiens

<400> 338

Phe Leu Tyr Cys Ala Cys Met Ser Pro Val Ile Thr Phe Gly Gly Leu
1 5 10 15

Leu Gly Glu Ala Thr Glu Gly
20

<210> 339

<211> 22

<212> PRT

<213> Homo sapiens

<400> 339

Ser Ser Ser Glu Ala Ser Val Cys Met His Leu Ser His Tyr Ser Tyr
1 5 10 15

Phe Tyr Leu Lys Ser Leu
20

<210> 340

<211> 106

<212> PRT

<213> Homo sapiens

<400> 340

Pro Cys Leu Gln Val Ile Gly Ile Asp Phe Cys Arg Leu Leu Leu Met
1 5 10 15

Cys Leu Val Leu Lys Arg Asn Leu Thr Val Pro Phe Ser Ser Tyr Ser
20 25 30

Pro Leu Lys Thr Ile Thr Cys Ile Thr Ser Glu Gln Ile Ala Val Val
35 40 45

Ser Asn Phe Phe Arg Gln Lys Leu Gly Val Arg Ala Lys Phe Phe Gln
50 55 60

Gly Ala Cys Leu His Thr Ser Lys Val Val Ile Cys Leu Asn Leu Pro
65 70 75 80

Ile Ile Ser Ile Gln Arg Ala Asp Ile Arg Met Trp Trp Leu Val Val
85 90 95

Asn Thr Pro Tyr Ala Arg Gly Val Asn Asn
100 105

<210> 341

<211> 21

<212> PRT

<213> Homo sapiens

<400> 341

Val Val Ser Val Cys Val Leu Glu Thr Gly Gln Leu Gly Pro Ala Ala
1 5 10 15

Leu Cys Arg Ser Val
20

<210> 342

<211> 97

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (28)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (79)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (83)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (85)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 342
Asn Ile Ser Val His Gly Phe Pro Val Pro Cys Leu Arg Gln Arg Leu
1 5 10 15
Gln Gly Pro Cys His Pro Lys Cys Cys Pro His Xaa Ile Ser Ser Gly
20 25 30
Lys Pro Arg Ser Ser Phe Ser Pro Ser Ser Tyr His Cys Lys Phe Ser
35 40 45
Arg Asn Ala Thr Leu Leu Val Val Pro Asn Ile Phe Ser Tyr Met Gln
50 55 60
Ser Ser Phe Leu Ile Pro Gln Thr Ser Lys Tyr Tyr Ile Leu Xaa Pro
65 70 75 80
Tyr Ala Xaa Thr Xaa Arg Pro Ile Lys Xaa Ile Phe Lys Gln Ala Lys
85 90 95

Gln

<210> 343
<211> 58
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (19)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 343
Ile Tyr Asn Asp Met Met Met Glu Lys Lys Lys Thr Glu Val Tyr Gln
1 5 10 15
Lys Arg Xaa Ser Gly Asp Asn Thr Trp Gly Gly Lys Gly Leu Val Ala
20 25 30
Phe Val Ser Ser Met Glu Gln Gly Ile His Val Gln Arg Cys Phe Ile
35 40 45
Ala Asn Leu Lys Phe Ser Ser Pro Gly Val
50 55

<210> 344

<211> 93
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (16)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 344
 Tyr Asp Asp Gly Glu Lys Glu Asp Arg Gly Leu Pro Glu Glu Met Xaa
 1 5 10 15
 Trp Gly Gln His Leu Gly Trp Gln Gly Pro Cys Ser Leu Cys Leu Lys
 20 25 30
 His Gly Thr Gly Asn Pro Cys Thr Glu Met Phe Tyr Cys Gln Phe Lys
 35 40 45
 Ile Phe Ile Ser Trp Cys Leu Ile Pro Leu Val Phe Ala Arg Leu Gly
 50 55 60
 Asp Phe Arg Asp Arg Pro Gly Trp Ile Phe Ser Trp Arg Tyr His Leu
 65 70 75 80
 Lys His Thr Val Trp Gly Gly Tyr Asn Ile Ile Met Leu
 85 90

<210> 345
 <211> 21
 <212> PRT
 <213> Homo sapiens

<400> 345
 Thr Pro Gly Asp Glu Asn Phe Lys Leu Ala Ile Lys His Leu Cys Thr
 1 5 10 15
 Trp Ile Pro Cys Ser
 20

<210> 346
 <211> 34
 <212> PRT
 <213> Homo sapiens

<400> 346
 Ile Arg His Glu Ile Phe Leu Thr Ile Glu Ser Phe Cys Pro Ser Ala
 1 5 10 15
 Pro Arg Gly Glu Asp Asp Asp Asn Leu Leu Arg Thr Ser Arg Val Pro
 20 25 30
 Asp Ile

<210> 347
<211> 160
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (126)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (130)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 347
Ile Arg Gly Ser Ile Pro Gly His Lys Lys Met His Leu Ser Phe Asn
1 5 10 15

Val Ala Ala Gln Trp Ser Leu Leu Lys Pro Leu Val Leu Arg Glu Glu
20 25 30

Gly Ala Leu Phe Leu Thr His Asp Gln Leu Glu Ser Lys Asn Ser Trp
35 40 45

Thr Leu Ser Ile Gly Pro Arg Val Pro Tyr Thr Tyr Val Val Val Thr
50 55 60

Trp Ser Ser Ala Leu Trp Asp Leu Pro Asn Gln Pro Leu Ala Gly Arg
65 70 75 80

Lys Glu Ser Gly Gly Ser Tyr Gly Pro Ile Ser Val Thr Gln Ser Pro
85 90 95

His Gln Ala Ala Leu Lys Trp Phe Ala Lys Lys Lys Gly Lys Gln Ser
100 105 110

His Ser Thr Val Gln Leu Ala Asn Ile Leu His Val Phe Xaa Ala Pro
115 120 125

Asp Xaa Tyr His Phe Val Asn Thr Ser Leu Gln Leu Phe Leu Glu Tyr
130 135 140

Thr Val Met Cys Met Leu Cys Glu Asn Lys Gln Lys Thr Leu Gly Arg
145 150 155 160

<210> 348
<211> 135
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (10)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 348

Glu Pro Glu Val Thr Gln Val Xaa Ser Xaa Glu Leu Thr Phe Gln Pro
1 5 10 15

Arg Lys Ala Gly Ala Lys Val Thr Ala Gly Lys Ser His His Gln Val
20 25 30

Ile His Trp Glu Phe Glu Ile Met Leu Ser Ser Tyr Ser Thr Asp Val
35 40 45

Pro Leu Trp Phe Leu Lys Phe Phe Ser Ser Asn Leu Pro Gln Thr Tyr
50 55 60

Phe Pro His Ser Gly Val Lys Lys Trp Gly Ser Cys Phe Ser Leu Pro
65 70 75 80

Trp Arg Asp Ser Pro Leu Thr Phe Ile Ser Leu Leu Ser Ser His
85 90 95

Leu Thr Thr Phe His Leu Tyr His Leu His His Gly Ile Ile Cys Leu
100 105 110

Gly Phe Ser Val Tyr Phe His Arg Ala Tyr Thr Ser Leu Cys Ile Leu
115 120 125

Glu Thr Ala Val Gly Ser Tyr
130 135

<210> 349

<211> 25

<212> PRT

<213> Homo sapiens

<400> 349

Trp Ser Leu Leu Lys Pro Leu Val Leu Arg Glu Glu Gly Ala Leu Phe
1 5 10 15

Leu Thr His Asp Gln Leu Glu Ser Lys
20 25

<210> 350

<211> 22

<212> PRT

<213> Homo sapiens

<400> 350

Trp Phe Ala Lys Lys Lys Gly Lys Gln Ser His Ser Thr Val Gln Leu
1 5 10 15

Ala Asn Ile Leu His Val
20

<210> 351
<211> 25
<212> PRT
<213> Homo sapiens

<400> 351
Ala Gly Lys Ser His His Gln Val Ile His Trp Glu Phe Glu Ile Met
1 5 10 15

Leu Ser Ser Tyr Ser Thr Asp Val Pro
20 25

<210> 352
<211> 26
<212> PRT
<213> Homo sapiens

<400> 352
His Gly Ile Ile Cys Leu Gly Phe Ser Val Tyr Phe His Arg Ala Tyr
1 5 10 15

Thr Ser Leu Cys Ile Leu Glu Thr Ala Val
20 25

<210> 353
<211> 19
<212> PRT
<213> Homo sapiens

<400> 353
Lys Arg Leu Thr Ile Asn Ala Arg Val His Leu Trp Thr Leu Lys Ser
1 5 10 15

Val Pro Leu

<210> 354
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 354

Glu Tyr Val Phe Asn Met Xaa Xaa Tyr Ser Lys Ser Arg Ala Ile Ser
 1 5 10 15

Pro Leu Ser Gly Pro Tyr Thr Pro Arg Gly Thr Thr Pro Leu Pro Ile
 20 25 30

Ile Pro Glu Pro Gly Ala Arg Gln Arg Asp His Pro Ala Ser Leu Lys
 35 40 45

Tyr Ala Lys Ile Ile Gln Thr Lys Leu Phe Ala Leu Pro Tyr Pro Lys
 50 55 60

Glu Thr Ser Met Lys Ala Val Ala
 65 70

<210> 355

<211> 65

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (15)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (25)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (26)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 355

Glu Thr Val Pro Pro Arg Ser Ser Gln Phe Leu Lys Ile Thr Xaa Gly
 1 5 10 15

Pro Ala Arg Ser Met Ser Leu Ile Xaa Xaa Ala Ile Gln Asn Pro Glu
 20 25 30

Pro Tyr Leu Leu Tyr Leu Ala Leu Ile Pro Gln Glu Ala Leu Leu Leu
 35 40 45

Tyr Leu Ser Ser Gln Ser Gln Val Pro Gly Asn Glu Thr Thr Pro Pro
 50 55 60

Val

65

<210> 356

<211> 101

<212> PRT

<213> Homo sapiens

<400> 356

Asn Glu Val Ser Phe Ser Leu Ser Leu Gly Phe Ser Pro Arg Glu Phe
1 5 10 15

Ala Arg Trp Lys Val Asn Asn Leu Ala Leu Glu Arg Lys Asp Phe Phe
20 25 30

Ser Leu Pro Leu Pro Leu Ala Pro Glu Phe Ile Arg Asn Ile Arg Leu
35 40 45

Leu Gly Arg Arg Pro Asn Leu Gln Gln Val Thr Glu Asn Leu Ile Lys
50 55 60

Lys Tyr Gly Thr His Phe Leu Leu Ser Ala Thr Leu Gly Gly Lys Gln
65 70 75 80

His His Asn Pro Lys Leu Ile Gly Cys Gln Thr Ile Gly Asn Asn Val
85 90 95

Lys Thr Arg Val Ala
100

<210> 357

<211> 75

<212> PRT

<213> Homo sapiens

<400> 357

Val Pro Tyr Phe Leu Ile Arg Phe Ser Val Thr Cys Cys Arg Leu Gly
1 5 10 15

Leu Leu Pro Arg Arg Arg Met Phe Arg Ile Asn Ser Gly Ala Arg Gly
20 25 30

Asn Gly Lys Leu Lys Lys Ser Phe Leu Ser Arg Ala Lys Leu Phe Thr
35 40 45

Phe Gln Arg Ala Asn Ser Leu Gly Glu Lys Pro Arg Asp Lys Glu Lys
50 55 60

Leu Thr Ser Phe Gln Ser Lys Arg His Lys Ile
65 70 75

<210> 358

<211> 63

<212> PRT

<213> Homo sapiens

<400> 358

Glu Met Ser Ala Val Leu Phe Asn Gln Ile Phe Cys Asn Leu Leu Gln
1 5 10 15

Ile Gly Ser Pro Ser Lys Glu Ala Asn Val Pro Asp Lys Leu Trp Gly
20 25 30

Lys Arg Gln Trp Gln Thr Glu Glu Val Leu Pro Phe Gln Ser Gln Val
 35 40 45

Val His Leu Pro Thr Gly Lys Leu Pro Gly Gly Lys Ala Lys Gly
 50 55 60

<210> 359
 <211> 99
 <212> PRT
 <213> Homo sapiens

<400> 359
 His Tyr His Gly Ser Gly Phe Leu Ile Lys Glu Phe Gly Ser Phe Leu
 1 5 10 15

Ser Leu Leu Cys Met Leu Ser Cys Pro Tyr Val Phe Cys His Gly Met
 20 25 30

Leu Glu Gln Glu Val Pro Ser Ser Val Val Ser Pro Ser Thr Leu Asp
 35 40 45

Phe Pro Thr Ser Arg Thr Val Asn Lys Phe Leu Phe Lys Leu Pro Ser
 50 55 60

Leu Trp Tyr Ser Val Ile Ala Thr Gln Asn Gly Leu Lys Gln Lys Ile
 65 70 75 80

Arg Glu Thr Phe Leu Phe Val Gln Phe Ser Gln Met Pro Arg Trp His
 85 90 95

Lys Leu Glu

<210> 360
 <211> 48
 <212> PRT
 <213> Homo sapiens

<400> 360
 Phe Cys Lys His Asn Gly Ser Lys Asn Val Phe Ser Thr Phe Arg Thr
 1 5 10 15

Pro Ala Val Leu Phe Thr Gly Ile Val Ala Leu Tyr Ile Ala Ser Gly
 20 25 30

Leu Thr Gly Phe Ile Gly Leu Glu Val Val Ala Gln Leu Phe Asn Cys
 35 40 45

<210> 361
 <211> 139
 <212> PRT
 <213> Homo sapiens

<220>

<221> SITE

<222> (28)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE

<222> (115)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 361

Met	Pro	Lys	Pro	Gly	Ala	Ala	Thr	Gln	Arg	Thr	Leu	Leu	Cys	Leu	Pro
1				5				10					15		

Arg	Leu	His	Pro	Ala	Ser	Gly	Pro	Pro	Leu	Pro	Xaa	Ala	Gly	Pro	Leu
			20					25					30		

Arg	Gly	Leu	Arg	Gln	Leu	Pro	Ala	Leu	Pro	Val	Pro	Ala	Ala	Ser	Cys
		35					40					45			

Arg	Arg	Arg	Pro	Ala	Pro	Arg	Leu	Cys	Ala	Ala	Gly	Pro	Cys	Thr	Val
	50					55					60				

Gly	Pro	Ala	Ala	Ser	Pro	His	Ala	Pro	Pro	His	Gly	Cys	Pro	Pro	Pro
65					70					75					80

Ala	Ser	Leu	Ala	His	Val	Ala	His	Arg	Gln	Ser	Val	Ser	Gly	Thr	Val
				85					90					95	

Cys	Leu	Gly	Leu	Arg	Asp	Gly	His	Val	Arg	Gly	Gly	Cys	Ala	Ala	Val
		100						105					110		

Arg	Gly	Xaa	Ala	Ala	Leu	Pro	Trp	Asp	Ala	Ala	Ala	Ala	Gly	Pro	Asp
		115					120						125		

His	Met	Gly	Val	Gly	Ser	Gly	Pro	Ala	Leu	Leu
	130					135				

<210> 362

<211> 35

<212> PRT

<213> Homo sapiens

<400> 362

Met	Trp	Gly	Gln	Pro	Arg	Pro	Val	Asp	Ser	Val	Trp	Ser	Ser	Ser	Ile
1				5					10					15	

Pro	Lys	Lys	Ser	Val	Glu	Ser	Asn	Asp	Asn	Lys	Ser	His	Leu	His	Lys
			20					25					30		

Arg	Glu	His
		35

<210> 363

<211> 26

<212> PRT

<213> Homo sapiens

<400> 363

Met Thr Thr Lys Ala Ile Phe Thr Lys Gly Asn Ile Asp Ser Leu Ser
1 5 10 15

Phe Lys Ser Asn Met Trp Ser Val Tyr Ile
20 25

<210> 364

<211> 26

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (3)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 364

Asp Ser Xaa Leu Asp Arg Arg Pro Ser Gly Pro Asp Val Lys Phe Leu
1 5 10 15

Ser Asn Lys His His Phe Ser Met Val Cys
20 25

<210> 365

<211> 84

<212> PRT

<213> Homo sapiens

<400> 365

Cys Leu Ala Glu Ala Val Ser Val Ile Gln Ser Ile Pro Ile Phe Asn
1 5 10 15

Glu Thr Gly Arg Phe Ser Phe Thr Leu Pro Tyr Pro Val Lys Ile Lys
20 25 30

Val Arg Phe Ser Phe Phe Leu Gln Ile Tyr Leu Ile Met Ile Phe Leu
35 40 45

Gly Leu Tyr Ile Asn Phe Arg His Leu Tyr Lys Gln Arg Arg Arg Arg
50 55 60

Tyr Gly Gln Lys Lys Lys Arg Ser Thr Lys Lys Lys Asp Leu Asp Gly
65 70 75 80

Phe Leu Pro Val

<210> 366

<211> 62

<212> PRT

<213> Homo sapiens

<400> 366

Leu Cys Ser Thr Pro Val Pro Thr Leu Phe Cys Pro Arg Ile Val Leu
1 5 10 15

Glu Val Leu Val Val Leu Arg Ser Ile Ser Glu Gln Cys Arg Arg Val
20 25 30

Ser Ser Gln Val Thr Val Ala Ser Glu Leu Arg His Arg Gln Trp Val
35 40 45

Glu Arg Thr Leu Arg Ser Arg Gln Arg Gln Asn Tyr Leu Arg
50 55 60

<210> 367

<211> 48

<212> PRT

<213> Homo sapiens

<400> 367

Ala Arg Gly Glu Thr Ala Tyr Asp Gly Ala Ala Val Glu Phe Gln Glu
1 5 10 15

Pro Leu Ser Ser Cys Leu Phe Ser Ser Leu Asn Pro His His Trp Pro
20 25 30

Thr Leu Gly Val Gly Arg Pro Val Met Leu Thr Leu Glu Asp Lys Asp
35 40 45

<210> 368

<211> 200

<212> PRT

<213> Homo sapiens

<400> 368

Glu Leu Leu Gln Cys Gln Met Leu Glu Ala Ser Thr Leu Ile His Leu
1 5 10 15

His His Pro Arg Pro Gly Phe Pro Ala Leu Cys Ser Phe Leu Gly Phe
20 25 30

Arg His His Leu His His Asp Ala Leu Cys Ile Arg Val Leu Pro Glu
35 40 45

Asp Leu Glu Ala Lys Leu Cys Val Ser Leu His Gln Leu Leu His Arg
50 55 60

Gly Leu Cys Leu Pro Gly Phe Gly Ala Ala Cys Pro Gly Asp Gln Gly
65 70 75 80

Ser Glu Asp Glu Ala Arg Pro Pro Ala Val Leu Arg Ala Val Ala Leu
85 90 95

Leu Arg Ala Gly Leu Arg His Leu Ser Val His Ser Gly Trp Tyr His
 100 105 110

Leu Pro His Ser Arg Asn Gly Leu Pro Leu Leu Ala Leu Val Val His
 115 120 125

Phe Pro Glu Tyr Gly Gly Gly Pro Arg Glu Pro Val Pro Gly Gln Ser
 130 135 140

Gly Glu Phe Gly Arg Arg Thr Glu Leu Ser Thr Lys Gly Asp Thr Gly
 145 150 155 160

Asp Ser Arg Asn Ser His Leu Ala Gln Asp Met Ala Ser Leu Pro Phe
 165 170 175

Phe Lys Pro Cys Glu Cys Thr His Val Ala Val Cys Ser Pro Pro His
 180 185 190

Pro Leu Cys Gln Tyr Leu Cys Leu
 195 200

<210> 369

<211> 28

<212> PRT

<213> Homo sapiens

<400> 369

Leu Gln Cys Gln Met Leu Glu Ala Ser Thr Leu Ile His Leu His His
 1 5 10 15

Pro Arg Pro Gly Phe Pro Ala Leu Cys Ser Phe Leu
 20 25

<210> 370

<211> 31

<212> PRT

<213> Homo sapiens

<400> 370

His Gln Leu Leu His Arg Gly Leu Cys Leu Pro Gly Phe Gly Ala Ala
 1 5 10 15

Cys Pro Gly Asp Gln Gly Ser Glu Asp Glu Ala Arg Pro Pro Ala
 20 25 30

<210> 371

<211> 27

<212> PRT

<213> Homo sapiens

<400> 371

Leu Ala Leu Val Val His Phe Pro Gln Tyr Gly Gly Gly Pro Arg Glu
 1 5 10 15

Pro Val Pro Gly Gln Ser Gly Glu Phe Gly Arg

20

25

<210> 372
 <211> 30
 <212> PRT
 <213> Homo sapiens

<400> 372
 Gln Ser Trp Thr Ala Pro Ala Ala Arg Leu Pro Met Ala Leu Pro Gln
 1 5 10 15
 Met Cys Asp Gly Ser His Leu Ala Ser Thr Leu Arg Tyr Cys
 20 25 30

<210> 373
 <211> 190
 <212> PRT
 <213> Homo sapiens

<220>
 <221> SITE
 <222> (32)
 <223> Xaa equals any of the naturally occurring L-amino acids

<220>
 <221> SITE
 <222> (47)
 <223> Xaa equals any of the naturally occurring L-amino acids

<400> 373
 Gln Ser Ala Ala Gln Trp Phe Trp Trp Pro Gly Arg Ser Ala Ser Leu
 1 5 10 15
 Gly Gly Ala Lys Gly Met Gln Pro Pro Ser Leu Ala Ser Trp Pro Xaa
 20 25 30

Pro Arg Ser Ile Arg Cys Leu Arg Ala Pro Ala Pro Cys Ser Xaa Pro
 35 40 45

Ser Ala Ser Ser Ala Ala Val Gln Val Ala Cys Cys Cys Ser Leu Ala
 50 55 60

Cys Cys Gly Pro Ser Arg Pro Ala Ser Gln Gly His Leu Arg Trp Asp
 65 70 75 80

Pro Tyr His Leu Ser Arg Asp Leu Tyr Tyr Leu Thr Val Glu Ser Ser
 85 90 95

Glu Lys Glu Ser Cys Arg Thr Pro Lys Val Val Asp Ile Pro Thr Tyr
 100 105 110

Glu Glu Ala Val Ser Phe Pro Val Ala Glu Gly Pro Pro Thr Pro Pro
 115 120 125

Ala Tyr Pro Thr Glu Glu Ala Leu Glu Pro Ser Gly Ser Arg Asp Ala
 130 135 140

Leu Leu Ser Thr Gln Pro Ala Trp Pro Pro Pro Ser Tyr Glu Ser Ile
 145 150 155 160

Ser Leu Ala Leu Asp Ala Val Ser Ala Glu Thr Thr Pro Ser Ala Thr
 165 170 175

Arg Ser Cys Ser Gly Leu Val Gln Thr Ala Arg Gly Gly Ser
 180 185 190

<210> 374

<211> 93

<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (59)

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 374

Gly Ser Thr Gly Leu Trp Arg Gly Asp Arg Gly Pro Ile Glu Gly Gly
 1 5 10 15

Pro Gly Met Leu Ala Leu Thr Asp His Ser Arg Pro Met Ser Ser Ser
 20 25 30

Arg Pro Pro Ala Pro Gln Gln Thr Lys Leu Thr Asp Leu Ser Arg Gly
 35 40 45

Leu Gly Pro Ser Gly Thr Gly Tyr Ser Val Xaa Gly Ala Ser Trp Pro
 50 55 60

Gly Trp Ala Val Ala Ser Pro Ser Leu His Gln Ala Lys Gln Ser Val
 65 70 75 80

Pro Ala Thr Arg Thr Thr Val Pro Leu Thr Val Met Gln
 85 90

<210> 375

<211> 27

<212> PRT

<213> Homo sapiens

<400> 375

Gln Trp Phe Trp Trp Pro Gly Arg Ser Ala Ser Leu Gly Gly Ala Lys
 1 5 10 15

Gly Met Gln Pro Pro Ser Leu Ala Ser Trp Pro
 20 25

<210> 376

<211> 29

<212> PRT

<213> Homo sapiens

<400> 376

Ser Ser Ala Ala Val Gln Val Ala Cys Cys Cys Ser Leu Ala Cys Cys
1 5 10 15

Gly Pro Ser Arg Pro Ala Ser Gln Gly His Leu Arg Trp
20 25

<210> 377

<211> 32

<212> PRT

<213> Homo sapiens

<400> 377

Val Ser Phe Pro Val Ala Glu Gly Pro Pro Thr Pro Pro Ala Tyr Pro
1 5 10 15

Thr Glu Glu Ala Leu Glu Pro Ser Gly Ser Arg Asp Ala Leu Leu Ser
20 25 30

<210> 378

<211> 26

<212> PRT

<213> Homo sapiens

<400> 378

Arg Val Ser Phe Pro Val Ala Glu Gly Pro Pro Thr Pro Pro Ala Tyr
1 5 10 15

Pro Thr Glu Glu Ala Leu Glu Pro Ser Gly
20 25

<210> 379

<211> 95

<212> PRT

<213> Homo sapiens

<400> 379

Ser Asn Glu Ile Leu Leu Ser Phe Pro Gln Asn Tyr Tyr Ile Gln Trp
1 5 10 15

Leu Asn Gly Ser Leu Ile His Gly Leu Trp Asn Leu Ala Ser Leu Phe
20 25 30

Ser Asn Leu Cys Leu Phe Val Leu Met Pro Phe Ala Phe Phe Phe Leu
35 40 45

Glu Ser Glu Gly Phe Ala Gly Leu Lys Lys Gly Ile Arg Ala Arg Ile
50 55 60

Leu Glu Thr Leu Val Met Leu Leu Leu Leu Ala Leu Leu Ile Leu Gly
65 70 75 80

Ile Val Trp Val Ala Ser Ala Leu Ile Asp Asn Asp Ala Ala Ser
 85 90 95

<210> 380
 <211> 33
 <212> PRT
 <213> Homo sapiens

<400> 380
 Pro Thr Arg Pro Val Leu Leu Leu Ala Ile Asn Gly Val Thr Glu Cys
 1 5 10 15

Phe Thr Phe Ala Ala Met Ser Lys Glu Glu Val Asp Arg Tyr Asn Phe
 20 25 30

Val

<210> 381
 <211> 93
 <212> PRT
 <213> Homo sapiens

<400> 381
 Asn Asp Lys Lys Leu Leu Phe Leu Lys Gly Phe Trp Ser Ser Leu Lys
 1 5 10 15

Asn Glu Thr Pro Pro Pro His Phe Arg Leu Arg Met Val Thr Gly Val
 20 25 30

Ser Cys Ser Gly Thr Leu Trp Cys Leu Ile Ser Gly Val Ala Val Thr
 35 40 45

Pro Leu Gln Ser Pro Gln Trp Gly Ser Tyr Thr Glu Cys Val Pro Pro
 50 55 60

Thr Glu Leu Pro Ile Ala Gly Pro Gly Ala Ser Gly Val Gln Ala Ser
 65 70 75 80

Leu Lys Ser Arg His Phe Val Ser Ala Ser Gly His Thr
 85 90

<210> 382
 <211> 65
 <212> PRT
 <213> Homo sapiens

<400> 382
 Ser Glu Asn Arg Ile Tyr Arg Asn Gly Leu Glu Lys Met Arg Arg Glu
 1 5 10 15

Val Thr Ile Gly Arg Ser Ser Ser Ile Cys Leu Asp Gln Gln Val Lys
 20 25 30

Ala Gly Asn Ala Val His His Gln Trp Leu Lys Tyr Val Cys Trp Met
35 40 45

Val Val Val Val Gly Gly Ser Gly Val Gly Asp Gly Gly Asn Leu Gly
50 55 60

Met
65

<210> 383
<211> 129
<212> PRT
<213> Homo sapiens

<400> 383

Asn Trp Ser Gly Arg Arg Leu Arg Met Trp Pro Ser Ala Ala Leu Ser
1 5 10 15

Pro Ala Val Ser Ser Pro Ala Leu Ala Leu Thr Ser Pro Pro Lys Pro
20 25 30

Leu Lys Gly Glu Val Trp Leu Arg Trp Lys Leu Leu Gly Ser Arg Ala
35 40 45

Val Gly Leu Phe Ala Phe Ile Ala Leu Gly Thr Gln Ser Pro Leu Leu
50 55 60

His Arg Ala Cys Leu Pro Val Arg Gln Ser Trp Gly Cys Ser Glu His
65 70 75 80

Lys Ala Tyr Pro Ile Leu Arg Leu Gln Pro Asp Leu Glu Thr Gln Val
85 90 95

Gly Pro Gly His Gly Val Asn Trp Asp Leu Arg Thr Gln Ile Arg Thr
100 105 110

Ile Gly Glu Leu Gly Gly Asp Gly Gly Cys Ser Glu Met Arg Pro Leu
115 120 125

Phe

<210> 384
<211> 123
<212> PRT
<213> Homo sapiens

<400> 384

Asn Leu Phe Ser Thr Pro Cys Lys Arg Gln Lys Leu Ile Lys Leu Glu
1 5 10 15

Trp Thr Glu Ala Pro Asn Val Ala Leu Arg Cys Ser Leu Ser Cys Ser
20 25 30

Leu Ile Pro Gly Leu Ser Pro Asp Leu Ser Ser Glu Ala Pro Glu Gly
35 40 45